The Veterinary Record

PATRON: HER MAJESTY THE QUEEN

VOL. 70 NO. 3 ISSUE NO. 4163 47-72

JANUARY 18th 1958

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No. 3 JANUARY 18th, 1958 Vol. 70

Registered for Transmission as a Newspaper *Price 2s. post free*

The Veterinary Therapeutic Testing Board

WE published last week a notice received from the Agricultural Research Council announcing the setting up of a veterinary therapeutic testing board. The B.V.A. has been active in this matter for a considerable time, and readers may wish to know a little more of the background of the subject which may justly be regarded as a most important one.

At a meeting of the Veterinary State Medicine Committee of the B.V.A. in April, 1953, the late Mr. J. R. Barker suggested that, having regard to the desirability of new therapeutic substances being made available for veterinary use, such materials might well be subjected to test if a suitable machinery could be devised. At a meeting of the B.V.A. Council which followed, Mr. Barker was strongly supported.

An approach was then made to the Lord President of the Council, with the suggestion that the time was opportune for the creation of a Veterinary Research Council who would handle the testing of new therapeutic substances as part of their work. The then Lord President, however, decided that the time was not opportune for such a Council to be set up, but forwarded the Association's suggestion of the testing project to the Agricultural Research Council. Thus was begun a series of discussions between the A.R.C., the B.V.A., and other interested bodies, the outcome of which has been the creation of the new Board.

The aim, of course, is to secure the impartial testing of new veterinary substances for the prevention or control of animal diseases, and such diseases may include those of domestic pets and other animals in addition to farm livestock. Tests may be undertaken at the request of a manufacturer, agent, or importer of the substance concerned, a recognised veterinary organisation, the A.R.C., or on the initiative of the Board itself. For all proposals made the Board's decision will be final.

Where the proposal comes from a manufacturer or trader information on the nature and composition of the substance must be disclosed to the Board. If a test is proposed by some other body the manufacturer concerned will be invited to disclose these details. When the Board has decided to have a test made a conference of all those interested will be called, and there will be present practising veterinary surgeons nominated by the B.V.A. who are willing to help in the test. Such conferences will elect a small working party to be responsible for the test itself. Arrangements for the publication of results have been agreed upon, and there will be suitable safeguards both to the interests of the wider public and of the manufacturers or traders.

The new Board, which has already held a preliminary meeting, comprises three representatives from the B.V.A. (Mr. E. Wilkinson, Dr. W. R. Wooldridge, and Mr. J. W. Bruford), one from the R.C.V.S., two from the Association of British Pharmaceutical Industry, two from the Pharmaceutical Society of Great Britain, one from the Medical Research Council, and three additional members two of whom, nominated by the A.R.C., are Dr. W. S. Gordon and Dr. R. Scarisbrick, both very well known within the profession. The lay Chairman is Mr. Michael Noble who farms in Scotland.

It is proper that a tribute should be paid to Dr. F. H. K. Green, who, as secretary to a similar organisation set up about twenty years ago by the Medical Research Council, has given most valuable help in the formative stages of the new Board, and who has been chosen to represent the M.R.C.

We feel it will be generally thought that an important step forward has been taken in the interests of animal health, and that it is a matter for great satisfaction that our own Association has been so intimately concerned from the beginning.

Symposium on Viruses*

(*Part Two*)

BY

J. B. Brooksby ; T. W. F. Pay ; W. F. H. Jarrett ; J. T. Stamp ; H. P. Chu ; J. G. Campbell

British Mucosal Disease

BY

W. F. H. JARRETT
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IN this paper to-day I wish to discuss four main points :—

(1) The diseases which are included under the generic term " Mucosal Diseases." (2) The disease which we have seen in this area. (3) The experimental disease which has been set up in calves and the little we know of the characters of the causal virus, and (4) The differential diagnosis.

The name " mucosal disease " is a bad one since lesions are not confined to mucous membranes and many other conditions affect primarily the mucosae. However, it appears to have come to stay and diseases belonging to the group have the common characteristics of (*a*) affecting cattle, (*b*) having at some time in their course a characteristic type of buccal ulceration, (*c*) producing a febrile response, (*d*) showing a diarrhoeic syndrome, and (*e*) having at some point a leukopaenic blood picture.

The history of work on this group of diseases really dates from 1946 when workers at Cornell (Olafson *et al.*, 1946) reported on a highly contagious disease of cattle occurring in New York State and which they called " virus diarrhoea." Later, a similar disease was reported from Indiana (Pritchard *et al.*, 1954) and a related condition from Iowa (Ramsey *et al.*, 1953), mucosal disease. Similar conditions have been reported in Britain (Dow *et al.*, 1956), Holland (Jensen, personal communication), and India (Pande, 1956).

Some confusion has arisen in consideration of the relationship of members of the group to each other due to the widely conflicting estimates of morbidity and mortality in individual herd outbreaks. For example, American mucosal disease was said to have a low morbidity but a high mortality, whereas virus diarrhoea (N.Y.) and virus diarrhoea (Indiana) have a high morbidity and low mortality. In our original observations we thought that British mucosal disease followed the American mucosal disease pattern, but repeated examinations of all animals of all age groups on individual farms has demonstrated that British mucosal disease has a very high percentage morbidity, but since most cases are very mild they may be easily missed on cursory examination. Similarly, the flagrant and easily recognised form of the disease is only seen in a small proportion of cases and is often fatal ; hence the apparent low morbidity and high mortality. A similar state of affairs is stated to exist in at least some outbreaks of American mucosal disease which have been studied thoroughly (Pritchard, 1955).

The following description, therefore, has been divided into two parts, the first pertaining to the fully developed case and the second to the much commoner mild form ; the pathological difference is merely one of degree.

The basic lesion is the small vesicle-ulcer. What is presumed to be the primary viral effect is confined solely to the epithelial cells and this explains the rapidity of appearance and disappearance of the ulcers if secondary breakdown does not take place.

Clinically, the first change noticeable is a small (5 mm. diameter) depressed red area on the buccal mucosa. Histologically (Fig. 1) this consists of vacuolation of cells of the Malphigian layer with early degeneration of the cell strata above this. This ballooning of cells increases in magnitude (Fig. 2) until the upper layer disappears and the prickle cells form a vesicle of cribriform appearance (Fig. 3). This appears clinically as an oval white fluctuant vesicle, most easily demonstrated by stretching and blanching the oral mucosa. This structure is easily ruptured (Fig. 4) when the typical small transverse red ulcer is produced. Polymorphs then invade the crater and this may be the extent of the progress of the lesion with healing supervening rapidly when a firm white spot on the mucous membrane remains. If bacterial colonisation occurs, further excavation ensues (Fig. 5) and the ulcer penetrates to the subepithelial tissues. This more persistent lesion has a granulating base (Fig. 6) but may become diphtheritic, *e.g.* an oesophageal lesion has been seen to erode the trachea and give rise to a necrotising bronchopneumonia. (These Figures face page 60).

In the severe cases these ulcers are most prominent on the lips (for illustrations see Dow *et al.*, 1956), dental pad, hard palate and cheeks in which positions they may coalesce to form extensive erosion but they are also found on the muzzle and nostrils and may affect the skin over the whole body, udder, etc. It should be stressed that ulcer formation occurs in waves at intervals and we have observed cases which were severely ulcerated and then healed, death taking place (from diarrhoea and dehydration) when only a few small ulcers were present in the mouth : this type of case would be difficult to diagnose if seen only in the terminal phase.

Similar ulcers commonly occur in the interdigital space ; careful washing is almost always necessary to reveal these. Associated foot changes are acute laminitis, purulent undermining of the horn of the hoof and fibrous thickening of the coronary band. Lameness frequently accompanies such lesions.

* Six papers presented to the Association of Veterinary Teachers and Research Workers on March 2nd, 1957. The first two papers were published on December 28th, 1957. Mr. J. T. Done's paper on " Rhinitis in Pigs " is being published in a more specialised journal.

At *post mortem*, in addition to skin and mouth lesions, multiple small erosions are often present throughout the length of the oesophagus and similar ulcers, which may be up to several inches diameter, are found in the rumen. Abomasal changes are mainly in the fundus and pylorus and range from pin-head size ulceration to stripping of large areas of mucous membrane.

Similar features may be presented in the intestine; cases exhibiting dysentery show large areas of haemorrhagic erosion, but many severely diarrhoeic cows have been examined in which the stomach and intestines appeared normal at autopsy. Histologically, areas of so-called catarrhal enteritis may be seen (this has also been reported from America) but caution is required in interpreting this since it is a feature of many " normal " bovine bow ls.

The alimentary lymph nodes may be moderately enlarged and oedematous showing non-specific cortical lymphocytolysis histologically.

Clinically such cases are dull and apathetic and usually show diarrhoea ; the latter may be intermittent but it is usually copious and persistent, resembling that of Johne's disease ; it usually leads to severe dehydration and death. At this stage pyrexia may be present but the temperature is usually normal. A persistent leukopaenia of the order of 3 to 4,000 white blood cells per cu. mm. and affecting all types of leukocytes may be observed but this is not a constant finding.

In the mild form ulcers are usually confined to the mouth, muzzle and nostrils although the feet may be involved ; the erosions are usually small in number. No other obvious signs may be present but often there is fever (104° to 105° F.), inappetence, scouring and drop in milk yield of 1 to 2 days' duration. It is emphasised that careful examination of the mouth is necessary in suspected outbreaks as only 5 or 10 ulcers may be present at one time.

Epidemiology

The initial source of infection in the farms we have studied has not usually been found but recently introduced animals have been suspected in some cases. Experiments have shown that in-contact infection is easily produced, the " incubation period " from introduction being from 7 to 9 days.

Several patterns of spread and severity of infection have been seen. On one farm the outbreak was ushered in by the successive deaths, after acute dysentery, of 6 yearlings in 6 weeks. Those examined showed typical lesions. They were first affected when at pasture and finally the remaining 14 were stabled. One died shortly after and at this time 2 others showed mild diarrhoea, one was anorexic and 12 had mild buccal ulceration. No further deaths occurred in this group nor were further symptoms seen. The dairy herd was examined closely and 3 animals were found to have mild scour, 2 showing buccal erosions. The calves at this time were all normal. One week later a large percentage of the cows had mild mouth ulcers and a winter scour type of syndrome was present in the dairy herd. Two calves now showed mild ulceration. After another week the condition in the dairy byre was disappearing but 10 of the 12 young calves showed ulcers. One cow which had been scouring died but was not made available for autopsy, and 6 months later no further trouble has been reported.

Other outbreaks have been of the winter-scour type with sometimes 2 to 6 per cent. of the animals developing the severe form 6 to 8 weeks later and dying subsequently. In yet other farms there has been a complete absence of severe complications.

During a recent parasitic bronchitis vaccine field trial in which the vaccine was administered orally we noticed in the course of bottling calves that mucosal disease was present in 5 of the 50 or so farms involved. This was fairly widespread in the herds but the farmers had not suspected any disease to be present. It is possible that the condition is quite widespread in an almost subclinical or mild form.

Since our own observations have shown that British mucosal disease is the cause of at least some so-called winter-scour outbreaks, we would be grateful for any information on the incidence of buccal ulceration in winter-scour outbreaks seen by practising veterinary surgeons.*

The Experimental Disease

We have now carried out over 100 experimental transmissions of this disease using spleen, blood and faeces from affected animals. Line passage has been carried out using Seitz and Gradocol filtrates and bacteria-free suspensions of these tissues. Suitable routes of infection are the intra-peritoneal, intravenous and intra-epithelial routes (tongue and mucous membrane of the lips).

Features of typical infections are shown in Graphs 1 and 2. The disease is usually mild although we have in a few cases produced severe ulceration lasting several weeks.

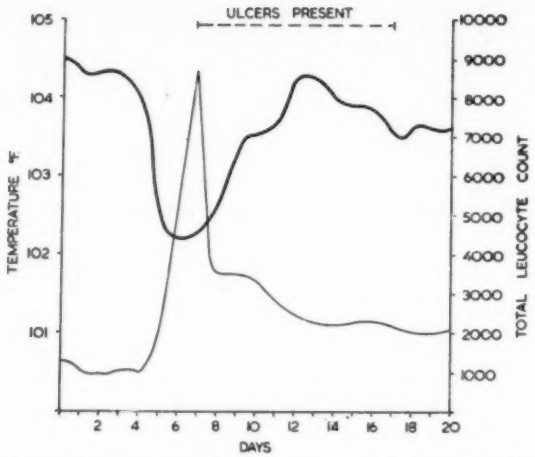
Animals after infection are usually resistant to further challenge after 40 days ; during this time they may still react (Graph 2) and an occasional case may show repeated ulceration over 2 months after only one infection. A sufficient number of animals is therefore necessary at each reinfection test to avoid false positive results. Temperatures must be taken 6 times daily at the period of expected febrile response. Cross-infection tests have shown no indication of more than one immunological strain being present.

In a severe case the spleen is infective at all stages of the disease, but in experimental cases we have been unable to demonstrate persistence of blood infectivity 4 and 8 weeks after infection. Spleen from the foetus of a calf aborted by an affected cow failed to induce the disease.

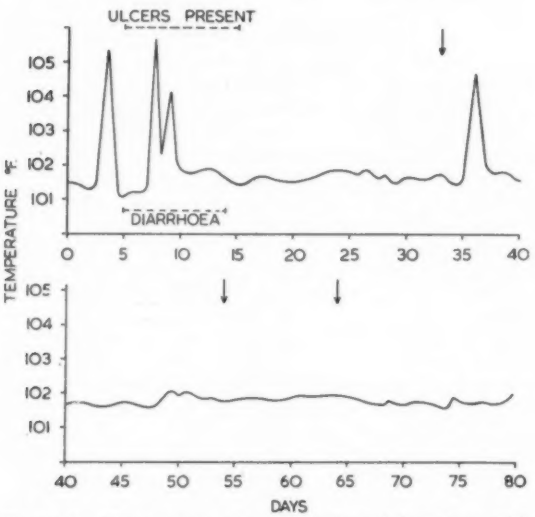
The virus is resistant to repeated freezing and thawing, citration, and storage for 16 months at –40° C.

A preliminary attempt to infect 3 sheep produced buccal ulceration in one and a febrile response in two. No back-passage into calves has yet been carried out with this material. Attempts to infect a goat, rabbits, guinea-pigs and mice (adult and suckling) have failed.

* Since this paper was read we have been able to study many outbreaks of " winter scour " and we are satisfied that it is a different condition from mucosal disease.



GRAPH 1.—The response shown by a calf inoculated intraperitoneally with a Seitz E.K. filtrate of spleen.



GRAPH 2.—The response of a calf challenged four times with the same virus suspension.

In preliminary studies using tissue culture techniques we have observed cytopathogenic changes in kidney monolayers. This material will shortly be tested for infectivity in calves and if possible may yield a suitable serological technique which is so badly needed in the study of this disease.

As yet we do not know the relationship between this condition and diseases of the American group. Freeze-dried virus has been sent to America for cross-immunity tests with their indigenous viruses.

Differential Diagnosis

The diseases which may present practical difficulty in Britain are foot-and-mouth disease, fascioliasis, Johne's disease and atypical winter ostertagiasis. By clinical examination and the appropriate tests the first three may be excluded but the last mentioned may be really difficult. However, the presence of buccal ulcers at one stage in British mucosal disease and the confining of the disease to winter and the young stock in atypical ostertagiasis are important points ; the abomasal lesions are also pathognomonic of the latter condition.

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Scrapie Disease of Sheep

A Review of the Contradictory Evidence as to the Nature of the Disease

BY

J. T. STAMP

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History

THE earliest definite record that has been found of the occurrence of scrapie in sheep in England was in 1732, but in 1755 the disease must have been very prevalent for a petition was sent to the House of Commons pointing out the seriousness of the disease and the economic losses which it was causing. During the 18th century the disease was well recognised and freely talked about in many parts of England for the symptoms were frequently described and the nature of the disease discussed both at agricultural meetings and in the agricultural Press. It seemed then to be known generally that scrapie affected all the breeds of sheep in the south of England and a goodly number further north as well. That the disease was indeed a serious menace to many flocks was well publicised for one can still read of the many statements made at that time such as " This disorder has been known to be fatal to the greatest part of a flock and is considered as the most calamitous circumstance the sheep owners have to dread " ; " The disease is so well known as not to require any particular description in this place " ; or " This malady is one of the most fatal that can happen in a flock," and many more of a similar nature could be quoted. During most of the 19th century the disease either became less common or was less freely talked about because it no longer was of topical interest in English farming circles. Towards the end of the century, however, the disease must once more have become serious, this time in the sheep flocks of the Scottish Border area, particularly in Northumberland and Roxburghshire, for frequent reference to it was made at the time by Border writers, and conversation now with older shepherds from these areas leaves no doubt that the disease was indeed prevalent.

Scrapie has also been well recognised in other European countries, Spain, Germany and France having had the disease for at least as long as Britain, if not longer. A number of writers have in fact suggested that the disease originated in these countries from the importation of Merino sheep from Spain during the 18th century, but Greig (1940) doubts whether this is so since he is not convinced that the disease was not endemic before the arrival of the Merinos.

Incidence

The incidence of scrapie disease in any flock at the present time varies considerably. In many affected flocks the number of cases of scrapie occurring in a year may be only 1 or 2 and this is often the case in commercial flocks selling cross lambs for slaughter where scrapie not uncommonly occurs in the breeding stock, especially in the purchased pedigree animals, either male or female. Since both the male and female lambs are sold off for slaughter the disease may be self-limiting in such flocks. Similar small numbers of cases occur in some hill flocks. On the other hand, and especially is this so in pure-bred flocks, the incidence of scrapie may be considerable and the numbers in any one year so numerous that the disease may be disastrous to the flock owner.

Scrapie is seen in a number of breeds of British sheep but it would be invidious to mention any breed as being particularly susceptible since the freedom of some breeds is perhaps rather apparent than real as the true incidence of the disease is normally a very closely guarded secret, shepherds often not even revealing its occurrence to the flockmaster. Contrary to general opinion, it can be said that the disease is by no means confined to the white-faced breeds of sheep although its incidence in the Scottish Blackface is thought to be very low.

Within recent years pedigree sheep exported from Britain to various scrapie-free countries have developed the disease at varying periods of time after reaching the importing country.

Age of Sheep Affected

The great majority of the cases occur when the sheep are 2 or 3 years old ; it occurs rarely in younger animals, but it is not infrequent in older ones. Both sexes may be affected, probably equally. In the female the development of symptoms is often related to pregnancy and lactation but many cases also occur at other periods, especially when feeding is intensive.

Aetiology

The cause of scrapie is unknown nor is there any definite knowledge regarding the spread of the disease; this is so despite the very considerable research work which has been carried out.

Until 1936 our knowledge of scrapie was based purely on observation of animals affected with the natural disease, but in 1936 Cuillé & Chelle claimed that they had transmitted the condition by injecting into healthy sheep, brain and spinal cord from a scrapied animal, the route of infection being intraocular, intracerebral, epidural and subcutaneous. This finding was later confirmed by Gordon (1946) and Wilson, Anderson & Smith (1950) ; the latter workers also transmitted the disease in series from sheep to sheep over 9 passages (Tables I, II and III). Wilson and his colleagues, using gradocol membranes, confirmed the earlier finding of Cuillé & Chelle that the transmissible agent could be filtered through virus filters. Wilson *et al.* (1950) interpreted these results to mean that scrapie was due to a virus infection of the central nervous system with an incubation period of 18 months to 5 years. The results of experimental work on grazing sheep on contaminated pasture gave Greig (1950) sufficient evidence to consider that the disease could be transmitted in this way. Wilson (1952), quoting unpublished work, stated that he had successfully transmitted the disease to sheep by subcutaneous, intravenous and intradermal inoculation of infective brain material while normal animals comparable in type and numbers to those used for inoculation never developed the disease when kept for 3½ years in the same environment as the inoculated animals.

Further experiments carried out by Wilson (1954) have shown that the transmissible agent is unusually resistant, and that amongst other things it can survive at 100° C. for 30 minutes. Gordon (1946) and Greig (1950) had already shown that the agent could resist a concentration of formalin of 0.35 per cent. over a period of at least 3 months.

Whether scrapie is in fact an infectious disease or not has long been debated and many flockmasters

TABLE I

THE EARLY EXPERIMENTAL EVIDENCE OF THE TRANSMISSIBLE NATURE OF SCRAPIE

			TRANSMISSION				
Total No. of Sheep	No. in Group	Age when Inocd	Inoculum	Route	Result	Time after Inocn	Author
9	7	Adult	Brain	Various	Intercurrent death	months 6-9	Cuillé and Chelle
	1	2½ yrs	Lumbar cord	Intra-ocular	Scrapie	14½	
	1	2	" (From natural case)	"	Scrapie	22	
8	No. 23	3 yrs	Cerebral	Epidural (Lumbar sacral)	Healthy	26	Cuillé and Chelle
	" 24	4-5 "	"	Subcutaneous	Intercurrent death	4	
	" 25	"	"	Intra-ocular	Intercurrent death	17	
	" 26	6 mths	Medulla	Epidural	Scrapie	12	
	" 27	"	"	Subcutaneous	Scrapie	19	
	" 28	"	"	Intra-ocular	Healthy	26	
	" 29	"	"	"	Healthy	26	
		"	Lumbar (From exptl. case)	Intracerebral	Scrapie	11	
	Lauping-ill Vacc	11 mths	Brain, spinal cord and spleen	Subcutaneous	5% scrapie (+35%)	2 yrs+	Gordon
788	788	Various ages	Brain and spinal cord	Intracerebral and subcutaneous	66% scrapie 34% scrapie	7 mths+ 18 " +	Gordon
29	20	Ewes	Pasture	Grazing	8 intercurrent deaths	Less than 4 yrs	Greig
					8 cases scrapie	4 yrs +	
	9	Lambs from above ewes	"	"	2 cases scrapie	18 mths	

TABLE II

PUBLISHED EVIDENCE REGARDING THE FILTRATION OF THE SCRAPIE AGENT

FILTRATION & TRANSMISSION

Total No of Sheep	No. in Group	Age at Inoculation	Inoculum	Route	Result	Time after Inoculation		Author
2	2	3 yrs. 4 mths.	Lumbar cord - Chamberland L 3 (From one natural case)	Intra-ocular and Subcutaneous	Scrapie	2 cases	16 mths.	Cuillé and Chelle
83			Cerebrum, Cerebellum, Mid brain, Medulla, Cervical cord (From one natural case)					Wilson, D. R.
	18	7 mths	Unfiltered	Intracerebral	Scrapie	4 cases	5–6 mths. (av. 5.7)	
	36	"	Gradocol (0.65μ A.P.D.)	"	Scrapie	10 cases	5–8mths (av. 6.30)	
	29	"	Gradocol (0.41μ A.P.D.)	"	Scrapie	7 cases	5–10mths (av. 6.32)	
	Cheviot wethers		(Animals were kept for one year after inoculation)					
15	3	2 Cheviots 17mths 1 Oxford X lamb	Gradocol (0.42μ A.P.D.)	Intracerebral	Scrapie	2 cases (in Cheviots)	5½ mths	Wilson, D.R.
	4	Oxford X lambs	Gradocol (0.20μ A.P.D.)	"	No cases of Scrapie	—	—	
	4	Oxford X lambs	Gradocol (0.12μ A.P.D.)	"	"	—	—	
	4	Oxford X lambs	Gradocol (0.055μ A.P.D.)	"	"	—	—	
			(Animals were kept for one year after inoculation.)					

both of the past and present hold the belief that scrapie is a disease carried in "the blood" or, in other words, that it is essentially a genetic condition and that the disease only becomes important when inbreeding is practised in a flock or in a breed. This hypothesis has been supported by a considerable amount of evidence from published and unpublished field observations but, on the other hand, an equally imposing variety of evidence can be found which opposes this view. The disease does seem to be much more frequent in pure-bred flocks and is reported to appear and disappear according to the extent of in-breeding practised which might suggest that inheritance plays a part in the aetiology. Recently Bosanquet, Daniel & Parry (1956) and Parry (1957) suggested that scrapie is an inherited defect and that many cases are but part of a more widely occurring inherited myopathy of sheep. They considered that the interpretation of the results of the above inoculation experiments purporting to establish scrapie as an infection of the central nervous system was open to question. In their opinion there are good grounds for suspecting that the so-called "normal" sheep used for the above experiments were not free from the myopathic trait in that they were mainly of a breed well known to suffer from scrapie and that the precautions taken to make certain that the animals were free of the disease were insufficient. They claimed that the failure of previous workers to recognise the presence of muscular lesions could be attributed to their preoccupation in recent years with the idea that scrapie was due to a transmissible agent affecting the central nervous system and to the fact that skeletal muscles are very seldom examined thoroughly at necropsy.

A leading article in *The Lancet* (1956), as a result of Bosanquet *et al.* findings, stated that it was clear that the data hitherto thought to establish scrapie as an infectious disease needed re-appraisal, and that veterinary police measures required reviewing since the sheep myopathies are probably hereditary in nature. It was also stated that at last a suitable experimental animal was available for the better understanding of the human myopathies.

The concept of scrapie being primarily a disease of muscle was of course first put forward by M'Gowan

TABLE III
SERIAL PASSAGE OF THE SCRAPIE AGENT

SERIAL PASSAGE (Wilson, D.R.)

(Intracerebral Inoculation of C.N.S. from Three Natural Cases)

	Positive			Negative	
Serial Passage	Breed	Age	Incubation Period (months)	Breed	Age
First	Cheviot	7 mths.	5	–	–
Second	Halfbred	1 year	4	Halfbred	1year
Third	Halfbred	5-6mths.	5	Halfbred Blackface	5-6 mths. "
Fourth	Greyface "	1 year "	6·25 3·75	Halfbred Greyface	1 year "
Fifth	Greyface " "	16mths. " "	4 4 5·75	Greyface	16mths.
Sixth	Blackface " Cheviot "	8mths. " 1year "	17·5 6·75 4·5 5	Blackface N.C. Cheviot "	8mths. 1 year "
Seventh	Cheviot " "	16mths. " "	4 6 5·5	Oxford X	4mths.
Eighth	Cheviot	10mths.	4·5	Cheviot " "	10 mths. " "
Ninth	Cheviot "	15mths. "	4·5 "	Cheviot "	15mths. "

in 1914 when he stated that careful clinical examination of typical cases of the disease made it highly probable that the symptoms of paralysis were due to a primary muscle lesion, but except for extensive sarcocyst infestation he was unable to find any muscle lesion even after careful *post-mortem* and histological examination. As a result of these findings M'Gowan put forward the suggestion that sarcosporidiosis was the essential cause of scrapie, a view strongly contested by M'Fadyean (1918) and by Stockman (1926).

In correspondence to the editor of *The Lancet* following the publication of the article by Bosanquet *et al.*, Pattison (1957) stated that in 1954 he inoculated 12 goats from the Compton flock intracerebrally with 1.0 ml. of a 10 per cent. brain emulsion from a sheep affected with scrapie. All 12 animals developed the disease, the earliest symptoms being noted 15 months after inoculation. He then inoculated 10 more goats with brain emulsion from one of the infected goats and up to the time of writing 8 of these have developed the disease. By contrast, over 650 other goats had passed through the Compton flock since 1949 without showing the slightest evidence of scrapie or other nervous disability. Pattison considered that this type of finding constituted evidence heavily in favour of scrapie being a disease that can be transmitted experimentally.

Recent work at Moredun (Stamp, Brotherston, Zlotnik & Smith, 1958) has confirmed and extended the earlier transmission work of Wilson (Table IV). Amongst other things it has shown clearly that the disease can be caused in about 30 per cent. of Cheviot & Blackface hoggs inoculated when 6 months old with a suspension of brain from scrapied Cheviot hoggs, whereas the inoculation of a similar suspension of brain taken from a number of normal Cheviot hoggs of the same age had no effect. The clinical signs of the disease in the injected sheep commenced when the sheep were all less than 12 months of age. No natural cases of scrapie occurred in normal controls of the same sample of sheep kept for 12 months after the experimental sheep were injected. Further, of 14 Cheviot lambs inoculated when less than a day old, 11 developed typical symptoms of scrapie when 3½ to 5 months of age.

Pathology

Macroscopic

Until recently all workers were agreed that there were no macroscopic lesions characteristic of scrapie but Bosanquet, Daniel & Parry (1956) described the

TABLE IV
RECENT EVIDENCE REGARDING THE EXPERIMENTAL TRANSMISSION OF SCRAPIE. (Present author.)

Type and Number of Sheep	Route of Inoculation	Sheep with Scrapie		Incubation Period	
		No	%	Case No	mths.
30 Cheviot wether hoggs	Intracranial (1ml.)	10	33⅓		
9 South Country		3	33⅓	1 2 3	5 5½ 5
21 North Country		7	33⅓	1 2 3 4 5 6 7	4½ 5 7 4 5 6 6
30 Blackface wether hoggs	Intracranial (1ml.)	7	23	1 2 3 4 5 6 7	5 5 5 5 5 5 5
30 Cheviot wether hoggs	Subcutaneous (5mls.)	9	30		
9 South Country		4	44	1 2 3 4	5 6 7 8
21 North Country		5	25	1 2 3 4 5	7 6 5 8 7
14 Cheviot day old lambs	Intracranial	11	79	3½ – 5 months	

post-mortem findings and histological examination of 48 cases of scrapie, part of a much larger group of scrapied sheep seen alive. In all cases examined in detail they found varying degrees of frank myopathy, the lesions being similar to those of polymyositis (dermatomyositis). The myopathic lesion took several forms, namely, diffuse and focal lesions of intense pallor, a translucency like the flesh of fish, firm pink lesions and excessive fat deposition. The lesion is usually bilaterally symmetrical. The myocardium is often involved and the adrenals enlarged.

Bosanquet *et al.* claim that myopathy provides for the first time a satisfactory explanation of most of the clinical signs of scrapie and that the lesion in the muscles is a primary intrinsic degeneration of the muscle fibres. Hulland (1958), however, working at the Moredun Institute and using considerable numbers of both natural and experimental cases of the disease has been unable to demonstrate the lesions of polymyositis (dermatomyositis) as described by Bosanquet *et al.*

Microscopic

In 1898 Besnoit & Morel reported the occurrence of vacuolated neurones in the medullas of sheep affected with scrapie and these observations were confirmed by Cassirer (1898) and later by Bertrand, Carré & Lucam (1937). Brownlee, in 1940, came to the conclusion that vacuolation of neurones in the medulla and cord was the only constant and specific lesion in scrapie. He did, however, report the occasional occurrence of vacuoles in sheep affected with other conditions, mainly louping-ill, but described these as being smaller and in necrotic cells, whereas scrapie vacuoles appeared in completely normal cells. Similar observations were made by Holman & Pattison (1943) who found vacuolation of neurones in all clinical cases of scrapie, very occasionally in sheep suffering from other conditions, and in one only out of 59 apparently normal sheep. They concluded that when clinical symptoms suggestive of scrapie are followed by microscopic discovery of vacuolated nerve cells in the medulla, this constitutes sufficient evidence on which to base a positive diagnosis of the disease.

Wilson, Anderson & Smith (1950) reported that in the medullas from sheep experimentally infected with scrapie, vacuoles were always present, but that in most cases a more searching examination was usually required for their demonstration than in material from sheep affected with natural scrapie.

At a later date Pattison (1957) using Zlotnik & Rennie's (1957) method of serial section examination gave details of vacuolation of the neurones in the medullas of goats suffering from experimental scrapie and gave figures which showed a statistical relationship between vacuolated nerve cells and scrapie, although similar vacuoles in very small numbers could be found in apparently healthy goats.

Zlotnik & Rennie (1957), carrying out extensive histological examinations of sheep brain found vacuolation and perivascular cuffing in a high proportion of normal animals of various ages of Cheviot sheep and concluded that, for a positive diagnosis of scrapie, vacuolation of neurones would have to be considerable, and the finding of several vacuoles in a single section of the medulla was of little significance. Examination of healthy sheep of the Scottish Blackface breed showed somewhat similar findings. Zlotnik (1957) examining two groups of sheep, one group consisting of 10 sheep in advanced stages of clinical natural scrapie and the other group being composed of 10 healthy animals of ages comparable to those suffering from the disease, gave results which showed that in the scrapied group the incidence of vacuolation of neurones in the medulla was very significantly greater than in the normal group. He pointed out, however, that the finding of even 7 vacuoles in an isolated section cannot be accepted as significant and that for the diagnosis of scrapie assessment of the number of vacuoles in serial sections of the medulla appears to be necessary. Bosanquet *et al.* (1956) examining the nervous system of scrapied sheep state that they found no obvious loss of anterior horn cells in the spinal cord, no inclusion bodies, no foci of nerve cell degeneration or of perivascular cuffing. The occasional vacuoles found in the large cells of the medulla and rarely in the anterior-horn cells of the spinal cord which have aroused so much interest in all workers on scrapie are, they believe, of little significance because they can be found in the nerve cells of normal sheep and of humans affected by various diseases.

Bosanquet *et al.* give a detailed description of the histological appearance of the degenerating muscle found in their cases of scrapie and conclude that the lesion is that of a primary muscle degeneration similar to a polymyositis (dermatomyositis) or to the more acute lesions of a muscular dystrophy.

Discussion

The nature of scrapie disease of sheep presents a fascinating but perplexing problem to the research worker. The conflicting evidence of the numerous investigations reviewed above appears to make confusion worse confounded.

Some facts are, however, indisputable. In the first place, scrapie can be made to occur in Cheviot and Blackface sheep and Compton goats within a constant period of months by the subcutaneous, intracranial or intradermal inoculation of filtered brain material taken from a sheep or goat showing clinical symptoms of the disease ; the disease can be transmitted in series, and the agent can be filtered through a virus filter ; temperatures of 100° C. acting on such an inoculum for considerable periods of time fail to destroy the agent as also does 0.35 per cent. formalin.

The resistance of the transmitting agent suggests that it is not likely to be an orthodox virus, but the fact that the disease can be transmitted in series (so suggesting a self-replicating agent) in sheep, goats and day-old lambs is difficult to explain on any other basis. Most certainly the assertion that cases of experimental disease are merely the development of natural cases of scrapie is not supported by the experimental data since symptoms occur in sheep of an age not normally affected, the incubation period after inoculation is constant and no case of the disease

has ever occurred in the numerous control animals kept for very considerable periods of time.

The recent suggestion by Bosanquet *et al.* (1956) that the disease is of genetical origin is based upon the finding of extensive lesions of myopathy in scrapie-affected sheep, the lesion in the muscles being described as a primary intrinsic degeneration of the muscle fibre. Since the epidemiological data of the disease in sheep is not comprehensive enough to establish that the sheep myopathies are genetically determined it is only by analogy with muscular dystrophy in the human that the conclusion is drawn that scrapie is possibly hereditary in nature. Since, however, the examination of the nervous system by these workers was not complete it is difficult to accept that the muscle lesions were in fact primary while in addition, as Walton (1956) points out, it is clear that much more information is necessary before the hypothesis that the sheep myopathy is akin to human muscular dystrophy can be accepted. The fact that neither M'Gowan (1914) nor Hulland (1958)—the latter after very careful and detailed examination of considerable numbers of undoubted cases of both natural and experimental scrapie—were able to find the muscle lesions as described by Bosanquet *et al.* throws some doubt on their conclusion.

Difficulty has also arisen as to the significance of the vacuolation of neurones in the medulla of scrapied sheep for Bosanquet *et al.* (1956) consider them of little importance while others, Holman & Pattison (1943) and Pattison (1957), are of the opinion that in scrapie an increase in numbers of vacuolated neurones is very significant. Zlotnik (1957) shows beyond doubt that this is so but also points out that for confirmatory diagnosis in many cases it is necessary to assess the number of vacuoles in serial section and not on a single section.

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Pleuropneumonia-like Organisms and Respiratory Diseases of Poultry *

BY

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I PROPOSE to start my talk by giving you a general account of pleuropneumonia-like organisms. I will then describe briefly the various respiratory diseases in poultry which may enter into our discussion and, finally, I will discuss the recent work on pleuropneumonia-like organisms in connection with respiratory diseases of poultry.

The Characteristics of Pleuropneumonia-like Organisms in General

So first of all, "What are pleuropneumonia-like organisms?" Our present knowledge of this group of organisms is still too limited for me to be able to give a satisfactory answer. I do not think I can do better than quote the criteria suggested by Sabin (1941) for the admission of an organism into the pleuropneumonia-like group. These criteria are: "(1) growth in cell-free culture media with the development of polymorphic structures including rings, globules, filaments and minute filterable elementary bodies usually 125 to 250 mμ in size, which are the minimal reproductive units; (2) the development on suitable solid media of characteristic minute colonies which may be as small as 10 to 20 μ and as a rule not larger than 600 μ." For the benefit of those who are not familiar with this rather inconspicuous group of organisms, I will try to explain these points more fully with the aid of some illustrations.

Pleomorphism is probably the most characteristic feature of pleuropneumonia-like organisms. This is well illustrated by the electromicrograph of a strain of goat pleuropneumonia-like organisms shown in Fig. 1, and by the photomicrographs of two strains of fowl pleuropneumonia-like organisms shown in Fig. 2. (*A number of the Figures referred to in this paper are printed in the art supplement in the centre of this journal.*) It can be seen that the organisms range from small particles of 200 to 300 mμ in diameter to larger bodies of variable shape and size. Filtration experiments confirm that the small particles represent the minimal reproductive units. As suggested by Kleineberger-Nobel (1954) the pleomorphism is mainly due to the lack of a rigid cell wall which would give the organisms a definite shape.

Because of their delicate structure, pleuropneumonia-like organisms are much more sensitive than bacteria to change in osmotic pressure and are thus readily distorted by the staining procedures usually employed for bacteria. Thus for the satisfactory demonstration of the organism the choice of fixative is just as important as the method of staining. In our experience, Giemsa staining after fixation with

* This work is supported by a grant from the Agricultural Research Council.

methyl alcohol, Bouin's solution or osmic tetraoxide gives the most satisfactory results.

The growth requirements of pleuropneumonia-like organisms are just as badly defined and variable as their shape and size. They will grow in cell-free media but the presence of serum and certain growth factors, including cholesterol and nucleic acids, are essential for the growth of most strains. The media usually employed consists of liver, heart or blood infusion to which peptone, yeast extract and serum have been added. Penicillin, thallium acetate or crystal violet are often included to check bacterial contamination. The media most widely used at present are probably those described by Edward (1947) and Smith & Morton (1951b). The latter has been prepared commercially in America and referred to as "Difco PPLO medium." It is, however, important to note that none of these media is specific for pleuropneumonia-like organisms alone, nor is it capable of supporting the growth of all pleuropneumonia-like organisms.

Thus an organism which grows in such a medium can only be identified as a pleuropneumonia-like organism after its morphology and its colony appearance on penicillin-free medium has been checked. Similarly, the failure to obtain a growth of pleuropneumonia-like organisms from infected material on one of the usual media does not necessarily mean that the material is free from pleuropneumonia-like organisms.

On solid media pleuropneumonia-like organisms produce tiny colonies rarely exceeding 0.5 mm. Under a dissecting microscope the colonies are characterised by the presence of a small nipple in the centre as shown in Fig. 3. Growth in liquid media produces only faint turbidity. Some strains grow in small clumps which either sediment to the bottom or adhere to the side of the tube.

Other characteristics of pleuropneumonia-like organisms include (1) their resistance to high concentration of penicillin and sulfa drugs, (2) their sensitivity to streptomycin, chlortetracycline*, chloramphenicol and oxytetracycline† and (3) their ready growth in chick embryos causing an irregular mortality of the embryos, especially following yolk sac inoculation.

The taxonomic position of pleuropneumonia-like organisms is still uncertain. Their ability to grow in cell-free media shows that they are definitely not viruses. On the other hand, in their morphology they resemble the viruses of the psittacosis group more than ordinary bacteria. They are generally regarded as organisms intermediate between viruses and bacteria. However, in their sensitivity to gold and arsenical drugs and the requirement of cholesterol as a growth factor they show some similarities to the protozoa. Under the electron microscope they are almost indistinguishable from Eperythrozoa. To me they seem to stand between bacteria, protozoa and viruses.

* Aureomycin. † Terramycin.

Before discussing the role of pleuropneumonia-like organisms in respiratory diseases of poultry it might be helpful to refresh our memories with what we know about the pathogenicity of pleuropneumonia-like organisms in general. There are only a few pleuropneumonia-like organisms whose pathological significance has been well established. These include the organism causing contagious pleuropneumonia in cattle and the two caprine pleuropneumonia-like organisms causing pleuropneumonia and agalactia in goats. In these diseases no infectious agents other than pleuropneumonia-like organisms have been found and the diseases can be reproduced by the pleuropneumonia-like organism cultures. Table I shows a list of other pleuropneumonia-like organisms isolated from various animals. Most of these organisms are suspected to be associated with some chronic pathological condition. But as similar types of organisms have also been found in apparently healthy animals their exact pathological significance is still uncertain.

For further information on this group of organisms three general articles recently prepared by Edward (1954), Kleineberger-Nobel (1954) and Edward & Freundt (1956) should be consulted.

A Brief Account of Various Respiratory Diseases in Poultry

Fig. 4 shows diagrammatically the long list of diseases which can affect the respiratory system of poultry and which clinically and pathologically can easily be confused with each other. This diagram was prepared to remind me of the complexity of the problem, and I was lucky enough to be made aware of this fact during the very first outbreak of respiratory diseases which I investigated. At that time I was only interested in Nelson's coryza, caused by coccobacilliform bodies, because of the relationship of these organisms to pleuropneumonia-like organisms. To my great surprise I was able to isolate *Haemophilus gallinarium*, infectious laryngotracheitis virus and pleuropneumonia-like organisms from the first infected chicken which I received from the field. This opened my eyes to the very important fact that in dealing with any one of the respiratory diseases in poultry, especially in the field, one must be alert to the possible complication by a host of other infections. It was clear that before starting any serious investigation of Nelson's coryza I must equip myself with the necessary knowledge and facilities to check the possible presence of other diseases. It was certainly not easy to do this single-handed, but subsequent experience has shown that the effort was worth while.

With the help of the diagram I will try to point out the main features of various respiratory diseases and the methods we have employed for their identification. For further information on these diseases, two recent general articles by Wilson (1954) and Gordon (1956) and two comprehensive papers on chronic respiratory disease by van Roekel (1952, 1953) should be consulted.

For the convenience of discussion, I divide the various respiratory diseases into 3 groups :—

TABLE I

PLEUROPNEUMONIA-LIKE ORGANISMS WHOSE PATHOLOGICAL SIGNIFICANCE IS STILL UNCERTAIN

Hosts	Organs affected	Associated pathological conditions	Other organisms associated with similar conditions	References
Man	Urino-genital tract	Chronic urethritis and cervicitis	Virus of inclusion blennorrhoea, gonococcus, *Trichomonas vaginalis*	Dienes (1940); Beveridge (1943)
	Joints	Arthritis	—	Dienes *et al.* (1948)
	Throat and saliva	—	—	Smith & Morton (1951a)
Pig	Respiratory tract	Atrophic rhinitis and pneumonia	—	Carter & Mckay (1953); Switzer (1953)
	Pericardial sac, pleural and peritoneal cavity	Pericarditis, pleurisy and peritonitis	—	Willigan & Beamer (1955)
Cattle	Genital tract	Sterility	—	Edward, Hancock & Hignett (1947)
	Respiratory tract	Bronchopneumonia	Pasteurella, corynebacterium	Carter (1954)
	Joints, kidneys and spleen	Arthritis and broncho-pneumonia	—	Moulton, Boidin & Rhodes (1956)
Sheep	Respiratory tract	Pneumonia	Pasteurella	Greig (1955)
	Feet	Foot-rot	*Fusiformis nodosus*	Beveridge (1941)
Dog	Respiratory tract	Laryngotracheitis and pneumonia	Distemper virus	Shoetensack (1934)
	Semen and vagina	Infertility	—	Edward & Fitzgerald (1951)
	Penis and prepuce sac	Balanitis	—	Chu & Beveridge (1954)
Mouse	Brain	Rolling disease	—	Findlay *et al.* (1938); Sabin (1941)
	Respiratory tract	Pneumonia and rhinitis	Pneumonitis virus	Edward (1940)
	Eyes	Conjunctivitis	—	Nelson (1950)
Rat	Respiratory tract	Infectious catarrh, otitis and pneumonia	Endemic pneumonia virus	Klieneberger & Steabben (1937)
	Joints	Polyarthritis	—	Findlay *et al.* (1939)
	Skin	Abscess	—	Woglom & Warren (1939)
Fowls	Respiratory tract	Chronic rhinitis, sinusitis, tracheitis, pneumonia and inflammation of air sac	Various respiratory viruses	Chu & Beveridge (1952); Markham & Wong (1952); Chu (1954)

Group 1. *Primary Respiratory Infections with well-defined Aetiology*

Haemophilus coryza is caused by a bacterium, *Haemophilus gallinarum*. Affected birds show nasal discharge, sinusitis and sometimes conjunctivitis and facial swelling. The incubation period is 1 to 2 days and the course of the disease varies. Diagnosis depends on the isolation from the sinus exudate of *Haemophilus gallinarum* which grows on chocolate agar in an atmosphere containing 5 to 10 per cent. CO_2. The disease responds favourably to treatment with sulfa drugs.

Infectious Laryngotracheitis. Infectious laryngotracheitis is caused by a filterable virus.

A typical acute outbreak of infectious laryngotracheitis is characterised by severe haemorrhagic tracheitis with high mortality. The affected birds show symptoms of gasping, mouth breathing, tracheal râles and coughing with blood-stained mucus. The disease, however, often occurs in a mild and chronic form. The affected birds show chronic pseudomembranous tracheitis not unlike that seen in fowl pox, vitamin A deficiency or chronic respiratory diseases. Diagnosis depends on the isolation of the virus on the chorioallantoic membrane of 10- to 12-day chick embryos. The virus produces pox-like lesions on the membrane. The lesions produced by infectious laryngotracheitis are usually more degenerative and necrotic and less proliferative and oedematous than those produced by fowl pox. Definite differentiation, however, depends on (1) histological examination of the infected membrane and (2) the inoculation of a suspension of the infected membrane on the comb and into the trachea of susceptible chickens. The presence of intra-cytoplasmic inclusion bodies in the section and the development of pox on the comb of inoculated chickens indicate that the virus grown on the chorioallantoic membrane is fowl pox. Absence of these lesions and the demonstration of intranuclear inclusion bodies in the section show that the virus is infectious laryngotracheitis.

Infectious Bronchitis. Infectious bronchitis is caused by another filterable virus, smaller than that of infectious laryngotracheitis. The virus can be grown in the allantoic sac of 9- to 11-day embryonated eggs. It does not produce pock lesions on the chorioallantoic membrane but it causes dwarfing, curling or death of the embryos. These effects are more marked after a few passages of the virus in chick embryos.

The virus affects chickens of all ages. Infectious bronchitis has a short incubation period of 1 to 2

days. If uncomplicated, the course of the disease is often not more than 2 to 3 weeks and the symptoms are usually confined to the lower respiratory passages. Some of the affected birds show gasping and râling. In laying hens the disease affects egg production and egg quality. Sometimes the disease in chicks and growers can be so mild as to escape notice. On the other hand, we have frequently noted outbreaks of infectious bronchitis complicated by secondary bacterial infections, including that of pleuropneumonia-like organisms. The disease then becomes chronic and the symptoms are more obvious, involving both the upper and lower respiratory tracts. Such outbreaks usually appear clinically more like chronic respiratory disease than infectious bronchitis.

Diagnosis of infectious bronchitis depends on (1) the isolation of the virus at the early stage of the infection by inoculating 8- to 10-day embryonated eggs *via* the allantoic cavity and (2) on the demonstration of neutralising antibodies in the infected birds.

Aspergillosis. Aspergillosis is caused by a green mould, principally *Aspergillus fumigatus*. The disease is characterised by the presence of cheesy nodules in the bronchioles, lungs and air sacs. Occasionally, greenish mycelial masses of the fungus are visible in the cheesy material. In adult birds the disease often occurs sporadically but in young birds the disease may be quite severe, affecting most birds in the brooder and causing high mortality. It is usually referred to as brooder pneumonia. Diagnosis

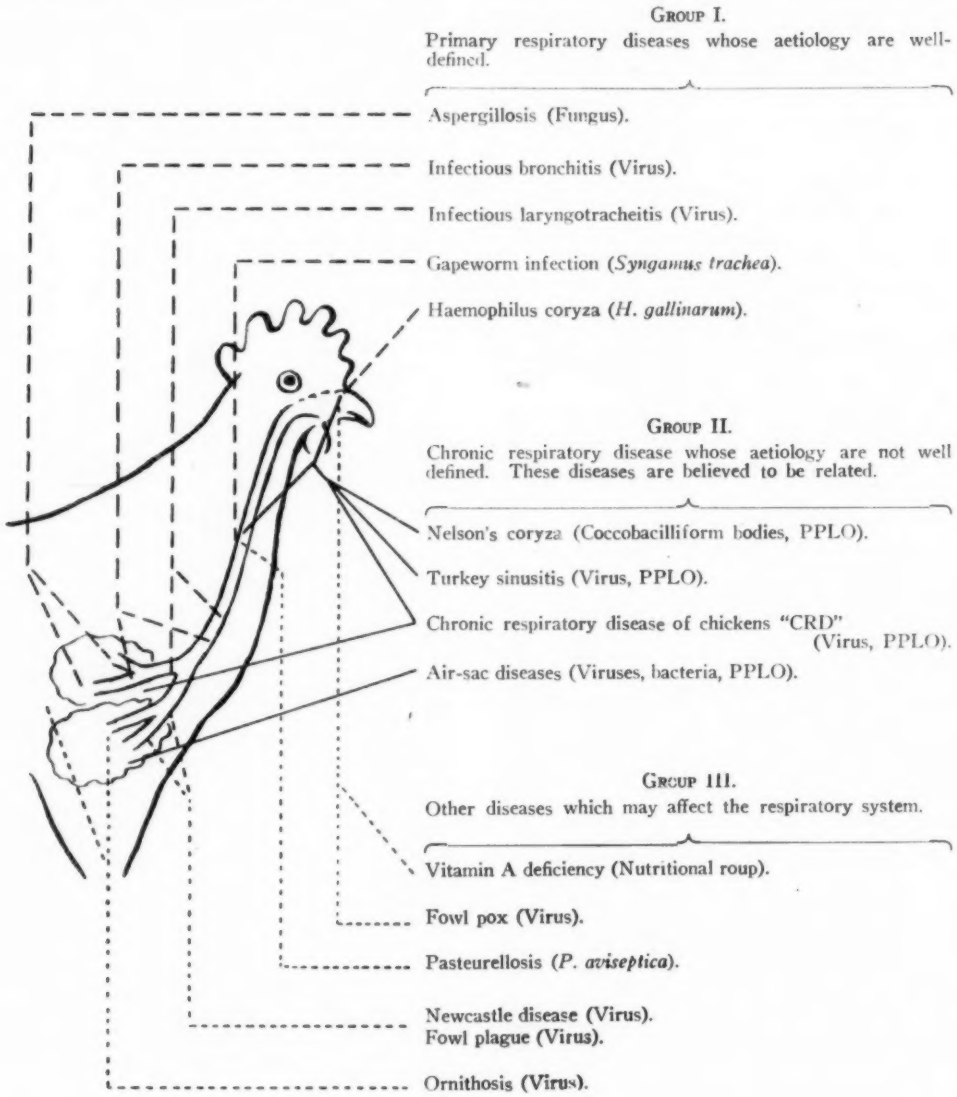

GROUP I.
Primary respiratory diseases whose aetiology are well-defined.
Aspergillosis (Fungus).
Infectious bronchitis (Virus).
Infectious laryngotracheitis (Virus).
Gapeworm infection (*Syngamus trachea*).
Haemophilus coryza (*H. gallinarum*).
GROUP II.
Chronic respiratory disease whose aetiology are not well defined. These diseases are believed to be related.
Nelson's coryza (Coccobacilliform bodies, PPLO).
Turkey sinusitis (Virus, PPLO).
Chronic respiratory disease of chickens "CRD" (Virus, PPLO).
Air-sac diseases (Viruses, bacteria, PPLO).
GROUP III.
Other diseases which may affect the respiratory system.
Vitamin A deficiency (Nutritional roup).
Fowl pox (Virus).
Pasteurellosis (*P. aviseptica*).
Newcastle disease (Virus).
Fowl plague (Virus).
Ornithosis (Virus).

FIG. 4.—Respiratory Diseases of Poultry.

depends on the demonstration of the hyphae of the fungi by microscopic examination of specimens treated with 10 per cent. potassium hydroxide and by the isolation of the organisms from the infected tissue using Sabouraud's medium.

Group 2. Chronic Respiratory Diseases whose Aetiology is not yet well defined

This group includes a number of chronic respiratory diseases which have many clinical and epidemiological features in common. Firstly, they all have a rather long incubation period, a very prolonged course and a chronic effect on growth and production and, secondly, they all seem to respond in a similar manner to a number of antibiotics. These diseases are : (1) Nelson's coryza of chickens ; (2) chronic respiratory disease of chickens ; (3) infectious sinusitis of turkeys, and (4) air-sac disease which is only a synonym of chronic respiratory disease. When they were first described, these diseases were thought to be caused by quite different agents, but recently it has been suggested that they are all probably due to pleuropneumonia-like organisms and represent the same disease. Although a lot of controversial problems have yet to be solved before a final conclusion on their relationship can be reached, it would be convenient to discuss them together.

Nelson's Coryza. This type of coryza was first described by Nelson (1935a, b, c). It differs from *Haemophilus coryza* described by de Blieck (1930) in having a longer incubation period of 1 to 3 weeks and a prolonged course of several months. Nelson showed that the disease was caused by a small gram-negative organism measuring 0.3 to 0.7μ which can be readily detected in smears of sinus exudate taken before complication by secondary bacterial infection. He called this organism the coccobacilliform body. He succeeded in growing the organism from the nasal discharge in Tyrode's solution, containing chick embryonic tissue, and in embryonated eggs. It is most remarkable that he was able to do this without the aid of antibiotics which are used nowadays to check bacterial contamination. He was able to reproduce coryza in chickens with his cultures. Later he showed that the organisms did not require living tissue for their growth and that they were probably related to pleuropneumonia-like organisms.

Nelson's coryza has since been identified by de Blieck (1948) in Holland and by us (1954) in this country. We have, however, noted in a small percentage of our infected birds, that the infection may spread from the nose and sinus to the trachea and air sacs (see Figs. 5 and 6). Coccobacilliform bodies can be demonstrated in Giemsa-stained smears of tracheal exudate as well as of sinus exudate (Fig. 7).

Chronic Respiratory Disease of Chickens. Chronic respiratory disease of chickens was first described by Delaplane & Stewart (1943) who showed that it was caused by a virus which can be propagated in embryonated eggs. Later, the mean diameter of the virus was shown by electron microscopy to be 53 mμ (Reagan, Brueckner & Delaplane, 1948). Inoculation of the so-called chronic respiratory disease virus or agent into 7-day embryonated eggs *via* the yolk sac caused an irregular mortality of the embryo from the 3rd day after inoculation up to hatching time. The lesions observed in the dead embryos include congestion, oedema and haemorrhage of the embryos, acute congestion and necrosis of the liver, congestion and haemorrhage of the kidneys, enlargement of spleen, pericarditis, inflammation of the respiratory tract with the accumulation of mucoid or cheesy exudate in the nose, trachea or air sac, and occasional arthritic lesions (Delaplane, 1949 ; van Roekel, 1952 ; Chute & Cole, 1954). Chronic respiratory disease is clinically and epidemiologically very similar to Nelson's coryza except that it involves also the lower respiratory passage. Affected birds often show tracheitis and air sac infection with or without coryza ; consequently, chronic respiratory disease is often referred to as air-sac disease.

In 1952 Markham & Wong reported the isolation of pleuropneumonia-like organisms, in Edward's pleuropneumonia-like organisms medium, from the yolk sac suspensions of chick embryos inoculated with egg passage strains of agents of chronic respiratory disease or turkey sinusitis, and succeeded in producing sinusitis in turkeys inoculated with the pleuropneumonia-like organism cultures after 13 consecutive passages in artificial media. Since then the study of chronic respiratory disease and turkey sinusitis has been centred on pleuropneumonia-like organisms and a large number of papers on this investigation have been published, especially in America. Time does not permit me to give an adequate review of this literature but I would refer you to a bibliography on chronic respiratory disease and turkey sinusitis recently prepared by Merck & Co. (1955) in which abstracts of 255 papers on these diseases are given. The introduction to this bibliography sums up the position regarding the aetiology of chronic respiratory disease and turkey sinusitis as follows. " The establishment of C.R.D. and turkey sinusitis as major diseases of poultry has focused the attention of poultry husbandrymen, pathologists, veterinarians and others concerned with diseases of fowls upon this infectious complex. The elucidation of its aetiology has been and still is in a state of flux, although it is generally agreed that a PPLO is the most likely cause. It is equally accepted that the causal agent is probably identical for both diseases." However, in 1954 a virus was isolated by Fahey & Crawley from field outbreaks of chronic respiratory disease. Inoculation of the virus into the yolk sac or allantoic cavity of embryonated eggs caused an early mortality of the embryos with a peak at 2 to 4 days after inoculation. The appearance of the dead embryos was similar to those dying from infection with the chronic respiratory disease agent. The virus also produced pock-like lesions on the chorioallantoic membrane. Intranasal inoculation of chickens with material containing the virus, or the virus plus pleuropneumonia-like organisms, produced respiratory symptoms characteristic of chronic respiratory disease. The virus was thus suggested to be involved in the aetiology of chronic respiratory disease.

In the past, the diagnosis of chronic respiratory disease depended mainly on the propagation of the agent from infected material in the chick embryo and its identification by the irregular mortality and the

lesions of the embryos. Recently, many workers have depended on the isolation of pleuropneumonia-like organisms in artificial media for the detection of chronic respiratory disease. From our experience of pleuropneumonia-like organisms in poultry I do not think that the isolation of these organisms alone from a chicken is specific enough to identify chronic respiratory disease.

Infectious Sinusitis of Turkeys. Infectious sinusitis of turkeys is a chronic respiratory infection normally affecting the nasal cavities, the infra-orbital sinuses and the eyes, but sometimes the lower respiratory passages are also involved. Clinically and epidemiologically the disease is very similar to Nelson's coryza or chronic respiratory disease. An organism which appears very similar to the coccobacilliform bodies of Nelson's coryza can be found in the sinus exudate of infected turkeys. However, this organism was first thought to be related to the viruses of the psittacosis group (Groupe, Winn & Jungherr, 1948) or rickettsia (Hitchner, 1949). Delaplane (1949) showed that the pattern of growth in chick embryos of Hitchner's S-3-400 turkey sinusitis agent is indistinguishable from that of the agent of chronic respiratory disease in chickens. The symptoms and lesions produced by the S-3-400 turkey sinusitis agent are also indistinguishable from those induced by the chronic respiratory disease agent. He suggested that these two diseases are probably identical. Markham & Wong (1952) showed that both turkey sinusitis and chronic respiratory disease agents can be propagated in Edward's pleuropneumonia-like organism broth and suggested that both agents resemble pleuropneumonia-like organisms.

Air-sac Disease. Air-sac disease or infection has been widely used as a synonym for chronic respiratory disease. This is rather unfortunate because the inflammation of air sacs associated with the presence of mucoid and cheesy exudate is a pathological condition rather than a disease entity. Such a pathological condition can be caused by a number of different agents. It would be advisable to discontinue the use of this name to avoid confusion.

Group 3. Other Diseases which may be confused with the above Primary Respiratory diseases

Apart from the above primary respiratory diseases there are still a number of other diseases which may also affect the respiratory system. Clinically they can be confused with the primary respiratory infections. This applies particularly to the following diseases.

Newcastle Disease. Newcastle disease, especially the mild form, can appear as a respiratory infection. Since Newcastle disease is a notifiable disease it is therefore important to rule out first the possibility of Newcastle disease in any outbreak of respiratory disease. This is usually done by means of the Haemagglutination Inhibition test using serum collected from infected birds. In some cases two successive tests may be necessary.

Fowl Pox. Fowl pox may occur in an atypical form without obvious lesions on the comb. The infection can easily be mistaken for infectious laryngotracheitis or infectious coryza. Definite diagnosis depends on isolation of the virus on the chorioallantoic membrane of chick embryos.

Vitamin A Deficiency. Vitamin A deficiency often appears like coryza. Typical vitamin A deficiency can be readily detected by the presence of pustules on the oesophagus. However, there are cases of mild deficiency in which these characteristic features are absent. In these cases the detection of deficiency depends on the estimation of vitamin A storage in the liver.

Psittacosis or Ornithosis. In dealing with outbreaks of lower respiratory infections, especially in turkeys, pigeons or ducks, it is important to watch for psittacosis or ornithosis as the disease may be infectious to man. Recently many outbreaks of turkey ornithosis were reported in America and the disease has been transmitted to workers in a poultry dressing plant (Pate, Boney & Delaplane, 1954). Detection of ornithosis is best accomplished by intracerebral inoculation of mice.

Pasteurellosis. Avian pasteurellosis can occur in a variety of clinical forms ranging from a chronic localised infection of the wattle and face with oedematous swelling to that of acute fatal septicaemia. The disease is rare in this country.

Routine Procedure for the Investigation and Diagnosis of an Outbreak of Respiratory Disease

In an outbreak of respiratory disease the first thing is to find out whether the disease affects principally the upper respiratory passage or principally the lower respiratory tract. This, together with the incubation period, the course of the disease, and the rate of spreading will provide a useful guide in diagnosis. For instance, if an outbreak affects mainly the upper respiratory passages with symptoms of nasal catarrh and sinusitis, and if it spreads slowly with a long incubation period of 1 to 3 weeks and a prolonged course of several months, it is more likely to be Nelson's coryza. On the other hand, if an outbreak affects mainly the lower respiratory passage with symptoms of gasping, rattling, coughing and mouth-breathing, with a shorter incubation period of 2 to 5 days and a shorter course of 1 to 3 weeks, and if it spreads rapidly, it is more likely to be infectious bronchitis, infectious laryngotracheitis or Newcastle disease. *Post-mortem* examinations should not be confined only to dead birds but, what is more important, they should be carried out on birds sacrificed at different stages of the infection. This is essential to give a complete pathological picture of the disease and to provide suitable material for the isolation of the various agents concerned.

There are certain clinical and pathological features which are diagnostic. Thus, if an outbreak of a lower respiratory infection is accompanied by nervous symptoms and haemorrhage of the proventriculus and intestine, then there is a strong suggestion of Newcastle disease. Similarly severe haemorrhagic tracheitis is characteristic of infectious laryngotracheitis and the presence of pustules on the oesophagus is pathognomonic of vitamin A deficiency.

Most of these diseases, however, occur in an atypical or mild form with the absence of the characteristic clinical or pathological pictures. For instance, nervous symptoms are often absent in the mild form

FIG. 1.—Vacuolation of Malphighian cells with overlying depression and degeneration.

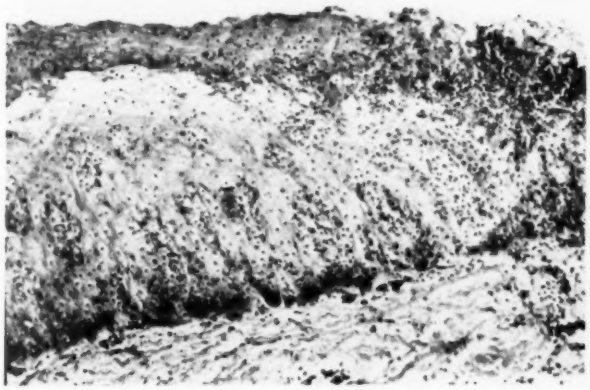


FIG. 2.—More extensive vacuolation.

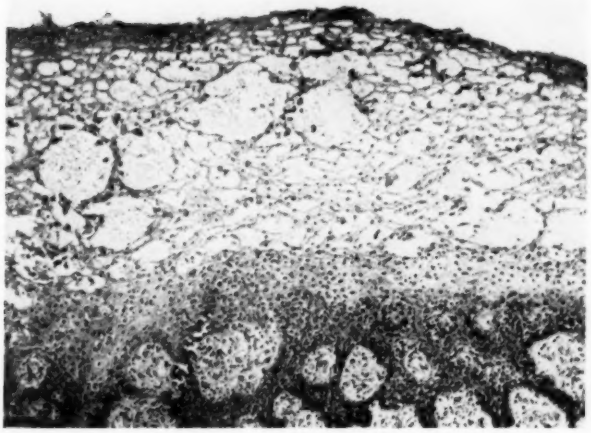


FIG. 3.—Intra-epithelial vesicle.

FIG. 4.—Collapse of vesiculated area.

FIG. 5.—Erosion of ulcer through epithelium.

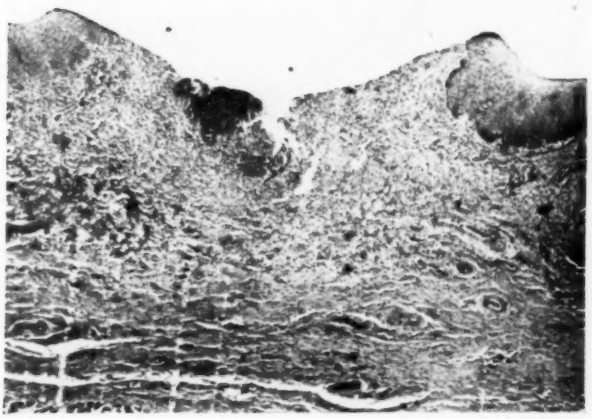


FIG. 6.—Granulating base of penetrating ulcer.

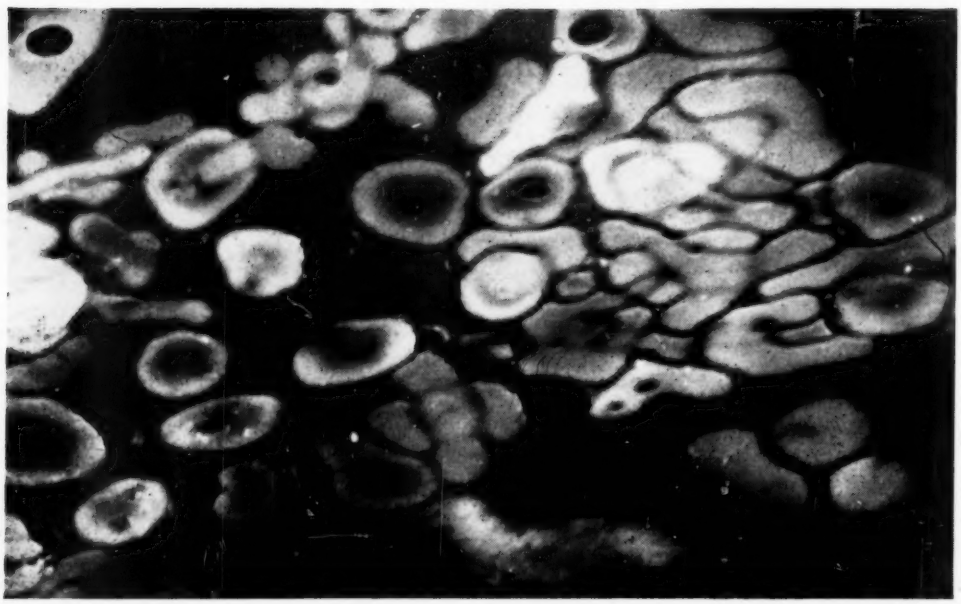


FIG. 1.—Electron micrograph of a stain of goat pleuropneumonia-like organisms showing the pleomorphism of the organisms. × 20,000.

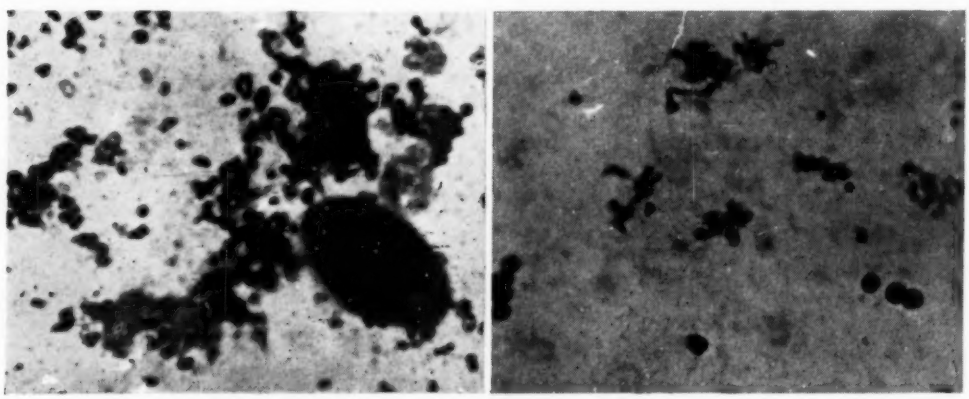
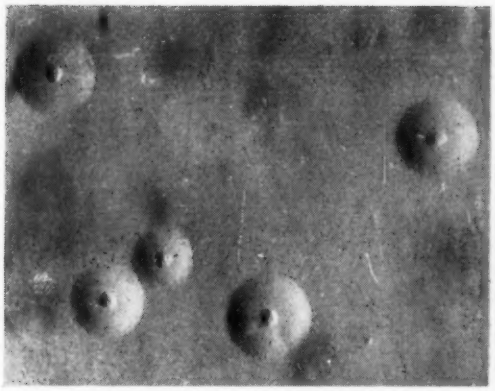


FIG. 2.—(*a*) A strain of fowl pleuropneumonia-like organisms grown in pleuropneumonia-like organisms broth, stained with Giemsa stain. Note the pleomorphism and compare their sizes with that of a fowl erythrocyte on the right-hand bottom corner. × 2,000.

(*b*) A Giemsa-stained smear of a culture of Nelson's coccobacilliform bodies. Compare the size with that of the Staphylococci on the lower part of the picture. × 2,000.



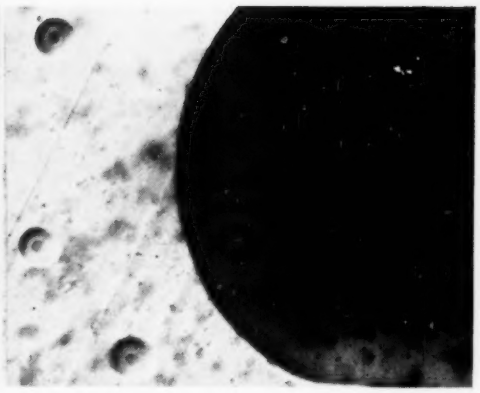


FIG. 3.—(*a*) The colonies of a strain of fowl pleuropneumonia-like organisms isolated from a case of infectious bronchitis. Note the presence of a nipple in the centre of the colonies which is characteristic of pleuropneumonia-like organisms. × 50.

(*b*) This photograph compares the size of colonies of a strain of fowl pleuropneumonia-like organisms with that of a colony of Staphylococcus. × 50.

FIG. 5.—A chicken affected with Nelson's coryza. Showing the presence of cheesy exudate in the infraorbital sinus.

FIG. 6.—A chicken affected with Nelson's coryza showing the spreading of the infection to the trachea and cervical air-sac. Coccibacilliform bodies can be found in both the sinus and tracheal exudate.
These pathological lesions are also characteristic of chronic respiratory disease of chickens.

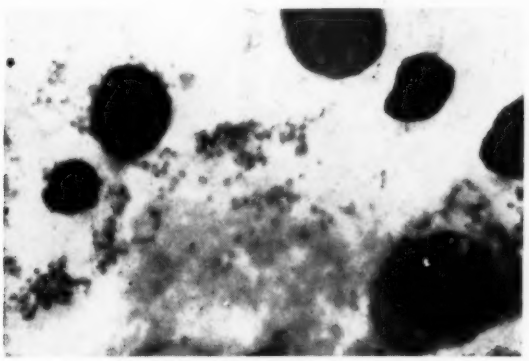


FIG. 7.—Smear of tracheal exudate from the chicken in Fig. 6 affected with Nelson's coryza. This shows the presence of a large number of coccobacilliform bodies.

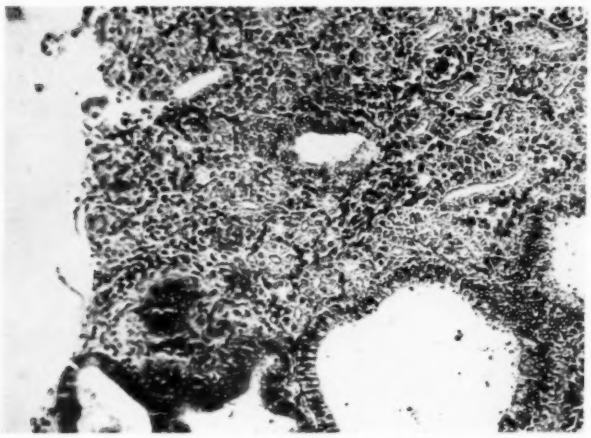


FIG. 1.—Early subcapsular cysts developing in the kidney of a chicken injected intramuscularly with 10 per cent. cell-free extract of erythroleucosis spleen. H. & E. × 150.

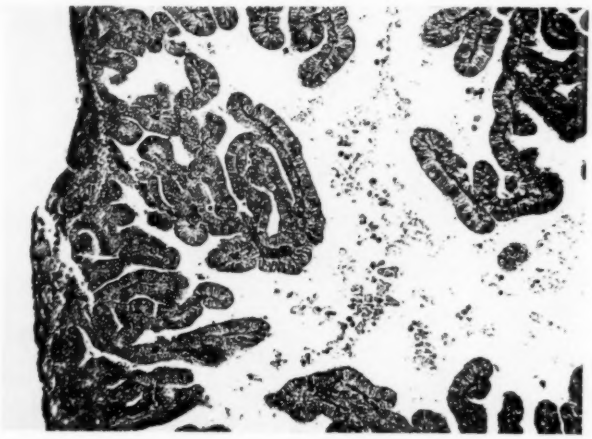


FIG. 2.—Fully developed cystic papillary adenoma of kidney in a similarly treated chicken. H. & E. × 96.

FIG. 3.—Detail of same. Trichrome × 300.

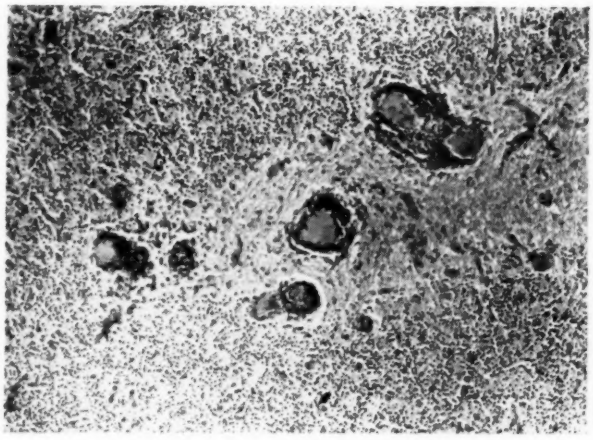


FIG. 4.—Experimental allergic encephalomyelitis. Advanced perivascular lymphoid cuffing in the white matter of the cerebellum. H. & E. × 108.

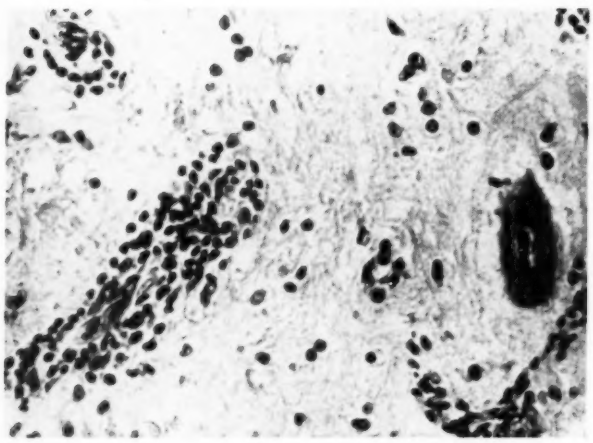


FIG. 5.—Experimentally produced early perivascular lesion, spinal cord. H. & E. × 510.

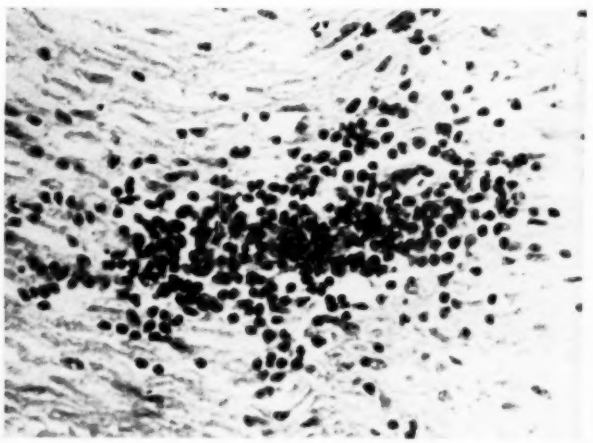


FIG. 6.—Mainly lymphocytic infiltration in sciatic nerve. H. & E. × 510.

of Newcastle disease ; mild infectious laryngotracheitis is often seen without the characteristic haemorrhagic tracheitis and high mortality ; while fowl pox without obvious pox lesions on the face and comb is frequently encountered. Outbreaks of infectious bronchitis or Newcastle disease can be so mild as to pass unnoticed and their presence is only suspected from the drop in egg production.

The frequent occurrence of these mild, atypical and chronic forms of disease has created a most difficult problem for the diagnosis and control of respiratory diseases in poultry. This shows that although the epidemiological, clinical and pathological findings can help a great deal in differentiating certain respiratory diseases, a definite diagnosis of a number of these diseases depends on the identification of the causative agent.

As a routine, the following procedures are used by us for the detection of the various viruses and other organisms which may be associated with an outbreak of respiratory disease :—

(1) Haemagglutination inhibition test for ruling out Newcastle disease. As a rule, this is done before we start our investigation.

(2) Smears of exudates from sinus, trachea, or other organs are made and stained by Giemsa's stain. The smears are examined for the presence of coccobacilliform bodies and for the checking of any gross bacterial contamination.

(3) Cultures of sinus and tracheal exudate are made on chocolate agar for the isolation of *Haemophilus gallinarum* and other bacteria. In a case of air sac involvement cultures are also made on MacConkey's agar for the colon group and on Sabouraud's medium for fungi.

(4) Inoculation into the allantoic cavity of six 9- to 10-day chick embryos of 0.1 ml. suspension of tracheal and sinus exudate in broth containing 1,000 units penicillin and 5 mg. streptomycin per ml. for the isolation of infectious bronchitis or Newcastle disease virus.

(5) Inoculation on the chorioallantoic membrane of six 11- to 12-day embryos of 0.05 ml. of a suspension of tracheal exudate or other appropriate infected material in broth containing 1,000 units penicillin and 5 mg. streptomycin per ml. for the isolation of infectious laryngotracheitis or fowl pox viruses.

(6) Inoculation into the yolk sac of six 6- to 7-day chick embryos with 0.1 ml. of a suspension of tracheal or sinus exudate in broth containing 1,000 units penicillin per ml. for the isolation of Nelson's coccobacilliform bodies, chronic respiratory disease agents or pleuropneumonia-like organisms. Another 6 embryos are inoculated with the same suspension to which a low concentration of streptomycin (0.5 mg. per ml.) is added. This concentration of streptomycin is usually not sufficient to inhibit most of the pleuropneumonia-like organisms, but sufficient to inhibit a number of contaminating bacteria.

(7) Neutralisation tests with serum collected from infected birds for infectious bronchitis and infectious laryngotracheitis.

(8) Transmission experiments in chickens and turkeys if necessary.

General Discussion on the Role of Pleuropneumonia-like Organisms in Respiratory Diseases of Poultry

The presence of pleuropneumonia-like organisms in poultry and their possible association with respiratory infection was suspected as early as 1936 by Nelson when he described a type of fowl coryza caused by a coccobacilliform body which has many similarities to pleuropneumonia-like organisms. Later in 1945, Van Herrick & Eaton reported the isolation of a pleuropneumonia-like organism from embryonated eggs during the passage of a pneumonia virus. The organisms produced haemagglutination which was inhibited by sera from a high proportion of hens in the hatchery providing the eggs.

It was only after the report of Markham & Wong (1952), however, when the causal agents of chronic respiratory disease of chickens and infectious sinusitis of turkeys were given as probable pleuropneumonia-like organisms that this group of organisms received a wide interest among poultry pathologists. Since then a large number of papers have been published on the subject, especially in America and Canada. My time will permit me to give you no more than some of their main findings :—

(1) Pleuropneumonia-like organisms can be isolated from cases of chronic respiratory disease in chickens and infectious sinusitis in turkeys as well as from laboratory strains of the causal agents of these diseases isolated from previous cases. Inoculation of these pleuropneumonia-like organisms in turkeys and chickens produces respiratory symptoms (Markham & Wong, 1952).

(2) The pleuropneumonia-like organisms isolated from chickens suffering from chronic respiratory disease and turkeys affected by sinusitis, as well as those isolated from pigeons and pheasants, are indistinguishable by cultural, morphological, biochemical, serological and pathological methods (Jungherr, Luginbuhl & Avampato, 1954 ; Gianforte, Jungherr & Jacobs, 1955 ; Fahey, 1954).

(3) Chronic respiratory disease of chickens and infectious sinusitis of turkeys are now generally accepted as being closely related, if not a single disease, and pleuropneumonia-like organisms are regarded as the most likely causal agent.

(4) The isolation of pleuropneumonia-like organisms in outbreaks of chronic respiratory disease in poultry has been used for the diagnosis of chronic respiratory disease or for the detection of carriers of chronic respiratory disease (Lecce & Sperling, 1954).

(5) Pleuropneumonia-like organisms or chronic respiratory disease agents have been shown to be transmissible through the eggs of infected hens (van Roekel, 1953 ; Fahey & Crawley, 1954b).

(6) Pleuropneumonia-like organisms isolated from chronic respiratory disease were shown to be susceptible *in vitro* to the action of a number of antibiotics, including streptomycin, oxytetracycline,* and chlortetracycline,† but treatment of outbreaks of chronic respiratory disease with these antibiotics have been rather disappointing (van Roekel, 1952 ; Yamamoto & Adler, 1956)

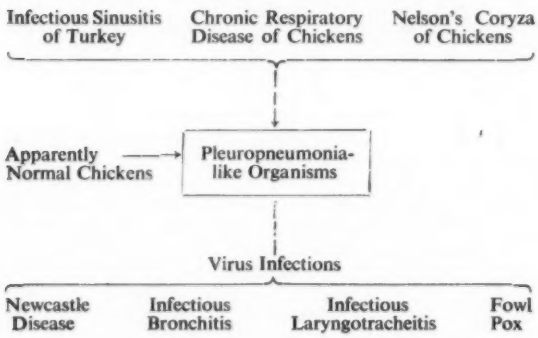
* Terramycin. † Aureomycin.

(7) A haemagglutination inhibition test (Jacobs, Jungherr, Luginbuhl & Gianforte, 1953) and a slide agglutination test (Adler, 1954) using pleuropneumonia-like organisms as antigen has been developed for the detection of chronic respiratory disease in flocks of chickens.

Based on the above findings it would appear that the problem of respiratory diseases in poultry is fairly simple. We already have the various specific means of identifying the various acute respiratory infections caused by viruses and bacteria. Now we are on the way to simplifying all the chronic respiratory diseases into a single disease likely to be caused by a single species of pleuropneumonia-like organisms for the identification of which, not only a simple cultural test, but also several serological tests have been developed.

In our experience the whole problem of pleuropneumonia-like organisms and respiratory diseases in poultry is much more complicated than has been suggested. This belief is based on our finding that the presence of pleuropneumonia-like organisms is not confined to chickens with chronic respiratory disease or to turkeys with sinusitis as shown in Fig. 8. We have been able to isolate pleuropneumonia-like organisms not only from chickens suffering from chronic respiratory diseases but also from those affected by practically all kinds of respiratory infections—infectious laryngotracheitis, infectious bronchitis and even acute Newcastle disease—and also from some apparently normal chickens. However, this does not necessarily mean that pleuropneumonia-like organisms are only innocuous commensal organisms ; it shows that the role pleuropneumonia-like organisms play in respiratory disease is not as straightforward as has been currently suggested.

FIG. 8.—PLEUROPNEUMONIA-LIKE ORGANISMS AND RESPIRATORY DISEASES OF POULTRY.



This diagram sums up the difficult problem concerning the role of pleuropneumonia-like organisms in respiratory diseases of poultry. It shows that pleuropneumonia-like organisms can be found not only in chickens suffering from those diseases which were supposed to be caused by pleuropneumonia-like organisms (namely Nelson's coryza, chronic respiratory disease and turkey sinusitis) but also from those affected with a number of other respiratory diseases caused by viruses which are found in some apparently normal chickens.

I would like to conclude my talk by presenting to you the problem as I see it, and our line of approach in tackling it.

Firstly, the isolation of pleuropneumonia-like organisms, either in artificial media or in embryonated eggs from chickens with chronic respiratory trouble, has been widely used for the diagnosis of chronic respiratory disease. To me, if chronic respiratory disease is identified or diagnosed on such a basis, we will be including under the name of chronic respiratory disease a wide variety of infections or mixed infections. Our experience in this country shows that in more than half of the outbreaks of chronic respiratory diseases from which pleuropneumonia-like organisms have been isolated, we were able to detect the presence of infectious bronchitis, infectious laryngotracheitis or fowl pox either by the isolation of viruses or by the detection of antibodies in the infected birds. Of the rest of the outbreaks, about a third were identified as Nelson's coryza by the demonstration of the typical coccobacilliform bodies in the sinus or tracheal exudate. This shows that chronic respiratory disease identified on this general basis can only be regarded as a clinical or epidemiological entity rather than an aetiological entity.

Secondly, our experience rather suggests that there may be more than one type of pleuropneumonia-like organism in poultry, and a specific type may be responsible for the uncomplicated chronic respiratory disease. The coccobacilliform bodies associated with Nelson's coryza might prove to be such a specific one. In fact we already have some evidence to show that the coccobacilliform bodies do differ considerably from the other pleuropneumonia-like organisms in their morphology, growth requirements and pathological effects on chickens and chick embryos. As mentioned in my previous paper (Chu, 1954) we had no difficulty in isolating some rapidly growing pleuropneumonia-like organisms from the sinus or tracheal exudate of chickens suffering from all kinds of respiratory diseases. These pleuropneumonia-like organisms usually produced visible colonies with a characteristic centre within 24 to 48 hours on Edward's pleuropneumonia-like organism medium and the organisms consisted mainly of rings, globules, bipolar bodies and a small number of coccobacilliform bodies (see Fig. 2a). On the other hand, with some sinus and tracheal exudate which contained a large number of coccobacilliform bodies we have experienced some difficulty in obtaining definite growths of pleuropneumonia-like organisms on Edward's medium (Chu, 1954). Later, from such material, we succeeded in obtaining the growth of some very fine colonies after a prolonged incubation of at least 4 to 5 days. Most of these colonies lacked the definite centre characteristic of pleuropneumonia-like organisms. The colonies consisted of organisms resembling the coccobacilliform bodies seen in the sinus and tracheal exudate (see Fig. 2b). With cultures of these organisms grown in Edward's medium we were able to produce coryza in about half of the chickens inoculated intranasally. Similarly, we have also noted that the slow-growing organisms of the coccobacillary type seem to affect the respiratory tracts of chick embryos more severely than do the rapidly growing

organisms. This is interesting in view of our failure to produce any respiratory symptoms in chickens inoculated with cultures of the rapidly growing pleuropneumonia-like organisms. This finding provides further support for our previous suggestion that there are likely to be different types of pleuropneumonia-like organisms or related organisms in poultry, some types being sufficiently pathogenic to cause disease by themselves, while others are only capable of acting as secondary invaders.

This suggestion, however, was contrary to the findings of Jacobs, Jungherr, Luginbuhl & Gianforte (1953), Gianforte *et al.* (1955) and Jungherr (1956) when seven strains of pleuropneumonia-like organisms 3 from chickens with chronic respiratory disease, 2 from turkeys with sinusitis, 1 from pheasants, and 1 from pigeons obtained from different geographic areas were shown to be identical on the basis of the results obtained from serological and chemical tests. These authors conclude from their findings that "it appears that, at least for the present, the possible aetiological agent of chronic respiratory disease exists as one species." Further work is now in progress in our laboratory to resolve this controversy.

Thirdly, if indeed all the pleuropneumonia-like organisms inhabiting the respiratory passages of fowls represent a single species, as shown by these workers, it would imply that any chickens which harbour pleuropneumonia-like organisms should be regarded as being infected with chronic respiratory disease or as carriers of the disease. In fact, a haemagglutination test and a slide agglutination test using pleuropneumonia-like organisms as an antigen have been used for the detection of these carriers (E. Gianforte *et al.*, 1955 ; Fahey & Crawley, 1954c ; Adler, 1954). Since some pleuropneumonia-like organisms which we isolated from chickens with fowl pox and acute Newcastle disease have been confirmed to be pleuropneumonia-like organisms by Edward & Freundt (who are 2 leading taxonomists) we are faced with the difficult problem of having to condemn our fowl pox or Newcastle disease infected chickens as carriers of chronic respiratory disease. This difficulty has been pointed out by Fahey & Crawley in their more recent paper (1956). These facts show that if there is really only one species of pleuropneumonia-like organisms in poultry, then these organisms alone are not likely to account for the whole aetiology of chronic respiratory disease. We have had to look for other more specific causal agents in addition to pleuropneumonia-like organisms. In fact, a new virus has already been identified by Fahey & Crawley in some outbreaks of chronic respiratory disease and we have shown that a number of known viruses such as infectious bronchitis virus and infectious laryngotracheitis are frequently associated with outbreaks of chronic respiratory disease. This is a problem of primary importance and of great general interest. Much more work is urgently needed.

Finally, as Nelson's infectious coryza, which is confined mainly to the upper respiratory passage, and Delaplane's chronic respiratory disease, which affects both upper and lower respiratory tracts, are now regarded as one disease caused by a single agent, we are left with some very interesting and important epidemiological questions to be answered. Firstly, in 1936 Nelson recognised the disease in America as a simple coryza, whereas, in 1943, Delaplane noted it as a more generalised respiratory infection ; still more recently the main emphasis in the description of disease has been on its involvement of the air sacs. Secondly, the disease occurs mainly in the form of coryza in this country, in the Netherlands and in many other countries, while in America it usually occurs now in the form of chronic respiratory disease affecting both the upper and the lower respiratory passages. The answer to these questions may be that different strains of the organisms concerned vary in their pathogenicity, or that different predisposing or aggravating factors are operating at different times and in different countries.

Among the possible predisposing factors I attach great importance to (1) the concurrence of other lower respiratory infections either as a result of natural infection or vaccination. (2) Overcrowding and bad ventilation associated with intensive poultry husbandry. These factors are likely to favour the spread of any upper respiratory infection to the lower respiratory passages. It is interesting to note that these factors are usually present in countries where chronic respiratory disease is more prevalent. In this connection I would like to emphasise that the control of chronic respiratory disease will depend as much on the elimination of these predisposing factors as on the elimination of pleuropneumonia-like organisms.

I hope that you will forgive me if you find at the end of my talk that I have succeeded in dragging you even deeper into the mire. The problem of colds in chickens is just as complex as that of our own common cold, and unfortunately our present knowledge is just not adequate to simplify it. I do not think I can honestly do more than present to you the complexity of the problem, the simplification of which depends not on my words but on more facts which will only emerge from much more work. In this connexion I am glad to mention that with the support of the Agricultural Research Council we have recently been able to expand our work to investigate more fully the problems mentioned in my talk.

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Recent Investigations on Avian Leucosis and Fowl Paralysis

BY

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AVIAN leucosis, associated as it is with the problem of cancer, offers one of the most challenging problems facing veterinary pathologists to-day. If it became possible at the present time to treat or control this group of diseases, not only would the poultry industry benefit to the extent of some £7,000,000 to £8,000,000 saved annually, as estimated recently by Blaxland (1956), but it is probably true to say that the whole of cancer research would receive a tremendous boost, comparable to that following the discovery of the effects of irradiation on tumours. The leucosis complex, as the term implies, covers a variety of conditions, not all of which, in the speaker's view, should be included. Over the years, workers from the other side of the Atlantic have tended to include neurolymphomatosis, iritis, and osteopetrosis in the complex, not always on the soundest of evidence, and a great deal of confusion has resulted from the general adoption of this scheme. This state of affairs has already been touched upon in previous papers (Campbell, 1954, 1956) and it is not proposed to pursue the matter further at the present meeting. It is sufficient to say that the leucoses proper are considered to be neoplastic conditions arising from haematopoietic tissues, and it is recent studies with these which will be mainly dealt with to-day.

The literature on the leucoses is extremely voluminous, and is widely scattered in a variety of journals, so it is no easy task to keep track with the latest developments. When it is recalled that Hungerford (1951) showed that 69 different synonyms in the English language alone were in popular use when describing these conditions, it is easy to see why this particular field of pathology is inclined to become a morass of confusion in which the worker may become hopelessly bogged down.

As already stated, the leucoses are regarded as being neoplasias of haematopoietic tissue origin, and as such comprise those conditions previously termed leucaemias or sarcomas if they happened to be unassociated with changes in the blood picture. As such, we have the 3 main groups :—

Erythroleucosis,

Myeloid leucosis,

Lymphoid leucosis,

and these may generally be either leucaemic in Virchow's sense, or aleucaemic, or both. In general, however, it may be fairly stated that the erythro form is usually leucaemic, the myeloid form may be both, and the lymphoid form is usually aleucaemic. The rare aleucaemic form of erythroleucosis is termed erythroblastoma, the aleucaemic form of myeloid leucosis may be either diffuse as in the condition affecting the viscera, or it may take a discrete tumorous form known as myelocytoma primarily associated with the bony skeleton of the thorax. The visceral and bony conditions are often present in the same individual. Lastly, the lymphoid form may also be diffuse or discrete, and in the latter case it is called lymphocytoma or visceral lymphomatosis. It is this last term which gives rise to most of the confusion between lymphoid leucosis and fowl paralysis, because the visceral form of the latter is also frequently termed visceral lymphomatosis. The illustrations for a previous article (Campbell, 1956) show certain fundamental differences which in my view justify restricting the term visceral lymphomatosis, well established by usage, to the aleucaemic form of

lymphoid leucosis, and introducing a new term, " lymphogranulomatosis," to cover the non-neoplastic visceral lesions often associated with fowl paralysis.

Erythroleucosis and Myeloid Leucosis

I will now deal with these conditions individually, commencing with erythroleucosis. This interesting condition was first described and named by Ellerman & Bang (1908), and thus became the first instance of a transmissible virus-associated neoplastic disease, even ante-dating by 3 years the classic Rous sarcoma series. Erythroleucosis often occurs together with myeloid leucosis (erythromyeloid leucosis) and until recently these two conditions were generally considered to be closely related, or even to have a common aetiological agent. Beard (1956) has now shown that it is possible to prepare the virus of myeloid leucosis in a pure form, and in a series of papers, has described its physical, chemical and antigenic properties, and he and his colleagues are now applying the same methods to the study of erythroleucosis. Thus it now seems that there are 2 agents and 2 distinct pathological conditions. Recently, further knowledge has been gained of what happens to the erythroleucosis virus upon introduction into the body (Campbell, 1954). It has been found that when a large dose of infective whole blood from a freshly dead bird is injected intravenously into young susceptible chickens, it remains demonstrable by sub-inoculation of blood from these recipients into a further series of susceptible birds for about 30 minutes after the initial injection. The infectivity then disappears, not to return demonstrably until about 18 hours later. In this latent or masked phase of the virus, not only is the blood uninfective, but also liver, spleen and marrow. This, then, apparently represents a phase comparable to that occurring in the replication of other viruses such as that of influenza, where the virus, after infecting the cell, breaks down into non-infective pro-virus, which multiplies and eventually reforms the complete infective virus. The phenomenon is of interest, since many cases of spontaneous leucosis do not have a demonstrable virus, and it seems possible that it is being held in an indefinitely prolonged masked phase.

The aetiology of lymphoid leucosis is a much more difficult problem, since only certain strains of the condition have been found to be associated with a transmissible agent, it being the experience of most workers that these tumours are usually not transmissible by filtrates or transplants. However, a strain was developed by Burmester *et al.* (1946) from a tumour isolated by Olson in 1941, which could be transmitted by filtrate, and a great deal of work has been done by Burmester using this tumour designated R.P.L. 12, as a result of which it is claimed (Cottral, 1952–4, and Burmester *et al.*, 1955) that egg transmission is the usual method of spread of this disease, which he terms " visceral lymphomatosis." All their results are based on studies on this particular tumour R.P.L. 12, which, in the hands of British workers does not seem to be associated with a virus (e.g. Darcel & Negroni, 1954) and indeed it is suspected by some that R.P.L. 12 is not a true lymphoid tumour, but an aberrant form of erythroleucosis. Whatever the truth of the matter it is obvious that a great deal more work needs to be done to clarify the position, especially as other workers, principally Cole & Hutt (1951) claim that leucosis is not egg-transmitted, a statement based on their work on " visceral lymphomatosis," which in their case appears to be identical with the various manifestations of fowl paralysis. Here again is an example of the confusion arising out of an inadequate system of classification, for while no question of the validity of their findings arises, yet two schools, working on what appear from their terminology to be identical conditions, produce conflicting results.

Although it is my contention that fowl paralysis should not be accepted as a part of the leucosis complex, yet it is perhaps inevitable that a few words about it are necessary, if only to emphasise the separateness of the condition. There is now ample evidence that fowl paralysis appears to be spread by contact in the field. Cole & Hutt (1951) have raised susceptible chicks in isolation, and shown they remain healthy. If at the end of 5 months they are brought back to infected premises they are found to be resistant, and experiments have shown that this resistance is attained in 10 to 16 weeks. They also show that the severity of the exposure to infection varies with the distance separating infected from non-infected birds, and have concluded that 3 factors are at work in the transmission of fowl paralysis, namely inheritance, age at exposure and severity of exposure. These same workers show that the condition can be spread by incubator or brooder contact, almost certainly by respiratory infection, and that the first 13 days of life are the most dangerous.

At this juncture it is perhaps fitting that a few observations should be made regarding some work with which I have been closely connected. Dr. J. G. Carr, at our B.E.C.C. Unit at the A.R.C. Poultry Research Centre in Edinburgh, has recently published (1956) some interesting experiments which indicate that the agents responsible for the leucoses do not exhibit such cellular specificity as some of us would like to think. By injecting certain graded doses of the erythroleucosis virus intramuscularly into young chickens of not more than 12 days old, he was able to prolong the onset of leucaemia in many instances to beyond its normal period for appearance. In those birds surviving say 3 to 4 weeks instead of the usual 7 to 12 days, a small proportion showed kidney tumours identified as papillary cyst adenomata of the cortex. The slides (Figs. 1, 2 & 3) show the structure of these tumours, and that they invariably arise from a sub-capsular position. Similar results were reported by Foulds (1934), using the Mill Hill virus associated tumour (M.H.2), although he concluded the renal tumours were atypically growing endotheliomata. Not unexpectedly, transplantation attempts result in erythroleucosis, since the birds are all infected with that virus. Carr concludes that the explanation may be that the kidney is embryologically derived from mesenchyme, and that up to 12 days certain foci of less differentiated renal " epithelium " persist and are susceptible to the action of the virus and so form neoplasms. Thus, while his findings show that the virus of erythroleucosis can act not only on haematopoietic tissue, but also on

another type of mesenchymatous cell, they do not support the view, occasionally brought forward, that even epithelial tumours may be caused by the agents of leucosis. With this observation, and the previously well-known one of the occasional induction of small fibro-sarcomata at the site of inoculation with erythroleucosis virus, we are forced to admit the widened potentialities of what has been conceived as a cell-specific agent.

Secondly, my colleague Dr. W. G. Siller, pathologist at the A.R.C. Poultry Research Centre, who is present to-day, has kindly allowed me to detail briefly some most interesting work now in progress which may have some connexion with the problems of neuro-lymphomatosis, or classical fowl paralysis. He has been able, by methods usually applied in allergy experiments, to produce a condition in fowls similar to experimental allergic encephalitis in mammals. By these methods, which will be published in due course, he has been able to produce typical fowl paralysis symptoms in a few birds, while in a further series of experiments, very suggestive peripheral nerve and brain lesions have been obtained. (Moreover, in 2 cases, the symptoms have been associated with nerve lesions. It is apparent that both the site of the lesion and its duration are important factors contributing to the complete picture.)

The following slides illustrate the pathology of the condition in nerves and brain (Figs. 4, 5 and 6) and again I am indebted to Dr. Siller for permission to show them.

Lymphoid Leucosis

Now, to pass on to another aspect of leucosis research, that is, investigations into the distribution of lymphoid tissue in fowls, and its relation to susceptibility. As is well known, birds have a diffuse lymphatic system in so far as lymphoid tissue is concerned, possessing no lymph glands, but only microscopic and widely scattered foci of germinal lymphoid centres. These have frequently been a stumbling block to comparative pathologists dealing for the first time with avian tissues, and have often been regarded as abnormalities. Lucas *et al.* (1949–50) in a series of papers have studied the character, number and total area of lymphoid foci, and shown that they increase with age and appear to bear some relation to a predisposition to develop lymphoid leucosis. He draws attention to a peculiar feature of some of these foci, which in perfectly healthy birds appear to possess invasive properties, and I can substantiate this interesting fact. The significance of this is difficult to assess unless such foci are in fact very early leucosis lesions.

It is pertinent here to mention some attempts to develop a method of diagnosing carriers of the leucosis complex. Kissling (1947) developed a leuco-agglutination test, based on the agglutination by the birds' serum of washed canine lymphocytes suspended and stained with methylene blue. He claimed to be able to detect a high percentage of infected birds by this test. Darcel (1950) repeated this work, and obtained an 80 per cent. agreement, but he remarked that the test seemed to be generally more specific for any form of gross liver damage. Field trials subsequently gave inconsistent results.

Another diagnostic test was developed by Mommaerts, Beard & Beard (1953). This is based on the observation that leucotic plasma possesses a higher adenosine triphosphatase activity than normal plasma which has virtually none. The test consists of measuring the speed of dephosphorylation of adenosine triphosphate by titrating the amount of acid liberated by the plasma enzyme in a certain time. Not much more information has been forthcoming since the test was announced, and so its reliability is difficult to assess. An interesting corollary to this is the observation of Mommaerts *et al.* (1952) that the enzyme seems to be integral with the leucosis agent, not being separable by washing, centrifugation or electrophoresis.

Treatment and Control

Finally, the question of treatment and control. Treatment is to date unsuccessful, and has included trials with an anti-metabolites such as aminopterin, A-methopterin and triethylenemelamine (Darcel, 1953) while Blaxland (1956) states that experiments with antibiotics and vitamins were uniformly negative.

Control offers more hope to date. Coles (1954) claims that isolation and genetic selection for 5 to 6 years is possible, but admits it is financially difficult. As fertile birds are the most susceptible, he says such selection could lead to fertility problems. Hutt & Cole (1954) dissent from these views. Waters (1954) selected birds for 14 years but could not obtain an absolute resistance against leucosis, and when he crossed resistant with susceptible stock no increased resistance was noted in the resultant line. He has recommended breeding from hens, not pullets, on the grounds that after the first year, these susceptible birds would be eliminated naturally. The drawbacks to this are said to include less prolific egg production, lowered fertility and lowered winter production.

Burmester & Waters (1955) tried to develop an immunity by means of a vaccine prepared from lymphoid tumours. The eggs from the vaccinated hens were incubated and the chicks challenged, resulting in a 3 to 13 per cent. mortality. Control chicks from unvaccinated hens showed a 41 to 70 per cent. mortality upon being challenged. They speak of working with "visceral lymphomatosis," but in fact used the R.P.L. 12 tumour whose identity is somewhat doubtful, as mentioned previously.

In the short space allowed, only a fraction of the work going on at the present time has been touched upon, and I hope you will therefore excuse this somewhat superficial survey. The whole problem is indeed enormous, but a step forward would be made if pathologists in every country could agree upon a classification which would dispel the present confusion caused so often by uncertainty in the reader's mind as to the actual identity of the condition being reported upon.

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(*Concluded at foot of adjoining column*)

Current Literature

ABSTRACTS

Demonstration of Specific Nerve Paralyses in the Dog. WORTHMAN, R. P. (1957). *J. Amer. vet. med. Ass.* **131.** 174–8.

The author describes the character of the paralyses that followed section of the major nerves to the limbs in dogs. Seventy-two neurectomies were experimentally performed in 49 animals : the nerves transected were the suprascapular, axillary, radial, musculocutaneous, median, ulnar, obturator, femoral, peroneal, tibial and sciatic. An illustrated account is given of the subsequent behaviour of the animals. This work is of value to those interested in peripheral nerve injuries in the dog.

Visna, a Demyelinating Transmissible Disease of Sheep. SIGURDSSON, B., PALSSON, P. A., & GRIMSSON, H. (1957). *J. Neuropath.* **16.** 389–403.

The authors describe a "slow," transmissible nervous disease of sheep which they regard as distinguishable from rida, scrapie and allergic encephalitis. The condition was transmitted by intracerebral inoculation of brain material and the earliest sign of infection was a pleocytosis, occurring about 2 months after inoculation. Clinical signs were aberration of gait, abnormal position of the head, trembling of the lips, paraplegia and sometimes total paralysis. No recoveries were recorded. Neuropathological changes were demyelination in the forebrain, cerebellum and spinal cord, and a meningeal and perivascular infiltration. Evidence is given that the disease is caused by a virus.

A.C.P.

Cat-Scratch Disease. HINDEN, E. (1957). *Brit. Med. J.* August 24th. 444–6.

Five cases of cat-scratch disease in human patients are described, 4 of these were in children and 1 in a woman in her late 50s. Two of the children are brothers but there was an interval of a year between the 2 cases and they were infected by different cats.

Four of the cases followed the pattern described by other recorders. In 1, however, the presenting signs were those of conjunctivitis and pre-auricular adenitis—a form of cat-scratch disease not previously reported in this country. It is suggested that the virus might be carried to the eye by the patient's own fingers and not introduced directly by the infecting cat.

Emphasis is laid on the difficulty of diagnosing cat-scratch disease and it is pointed out that diagnosis must rest on a consideration of all the data, epidemiological, clinical and pathological.

Cat-Scratch Disease with Pneumonia. SHELDON, G. C., & SMELLIE, H. (1957). *Brit. med. J.* August 24th. 446–7.

This report describes the case of a woman of 46, who worked in a household possessing an ageing cat. This animal was not house clean, and the patient had the unpleasant duty of cleaning up after it. She was never bitten or scratched by it.

In July, 1956 a small lesion developed on the palm of her left hand. In September the epitrochlear and axillary lymph nodes were enlarged, the lesion on the palm being an infected papule, there had been a transient lymphangitis. Under antibiotic therapy slow progress was being made when the patient became very ill with pneumonia. Recovery under antibiotic therapy was slow, but in 2 months the patient was discharged from hospital much improved. The local lesions disappeared without suppuration but a small pleural shadow at the left base remained. An intradermal injection of cat-scratch antigen produced an area of induration and erythema.

Pneumonia complicating cat-scratch disease has not previously been recorded.

The cat was destroyed within a month of the onset of the patient's illness. *Post-mortem* examination revealed no signs of disease. No virus was isolated despite a most exhaustive search.

G.F.B.

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News and Comment

R.C.V.S FELLOWSHIPS BY ELECTION

At the most recent meeting of the Council of the Royal College of Veterinary Surgeons it was unanimously resolved that the Fellowship of the College by election be bestowed on Professor W. L. Weipers, B.SC., M.R.C.V.S., D.V.S.M., F.R.S.E., and on Dr. W. R. Wooldridge, PH.D., M.SC., M.R.C.V.S., F.R.I.C.

It is understood that the Diplomas will be awarded at the Annual General Meeting in June.

PRODUCTION EXPERIMENT IN DEVON

Research into the factors which may be limiting production and profits on British farms will be carried out in the Teign Valley area of Devon by the Nuffield Foundation, who will spend £20,000 on it.

In announcing this at a dinner of the Hampshire branch of the National Farmers' Union, Mr. L. Farrer-Brown, director of the Nuffield Foundation, said that the project would be a practical research programme lasting 5 years.

The aim of the experiment would be to strive for greater efficiency in the use of scientific discoveries. "Obviously agriculture needs more scientific research. But it needs also, many knowledgeable people would say, to exploit fully the discoveries that science has already made available. What can be done about it? The new project is to seek answers to this kind of question by local experiment."

Bristol University is providing an agricultural economist to help with the experiment.

THE BRITISH SMALL-ANIMAL VETERINARY ASSOCIATION

This Association proposes to hold a congress on March 28th, 29th, and 30th, where papers will be presented and discussions take place on a wide range of subjects of interest to practitioners and other workers in the small-animal field.

The congress will be held in the Shaftesbury Hotel, Monmouth Street, London, W.C.2, and in addition to the scientific programme a certain number of social functions are being arranged.

A list of the subjects to be discussed, either in Papers or directly, is as follows:—

Blood transfusion in the dog; Treatment of shock; Current research in small-animal diseases; Ailments of cage and aviary birds; New techniques in small-animal surgery; Use of cortisone and allied drugs in small-animal practice; Recent advances in diagnosis of pseudo Hodgkin's disease, pancreatic conditions, hip dysplasia; Use of myelography and pyelography; Eye conditions in the dog and cat, current methods of therapy; The Association and other professional bodies, with special reference to our relationship with the B.V.A.; New techniques in small-animal surgery and anaesthesia, with special reference to equipment; The B.S.A.V.A. —its members and the welfare clinics; Design of small-animal premises and kennels; Laboratory aids to clinical small-animal medicine, urine analysis, blood analysis, biopsies, etc., and their application in general small-animal practice.

For those who find it impossible to attend all the sessions it is proposed that the chairman and recording secretaries prepare a short summary of all discussions for presentation to the general meeting which is to be held on Sunday, March 30th. It is hoped to tape-record the entire congress and the publication of proceedings will follow in the Association's bulletin.

All members of the profession will be welcome, but non-B.S.A.V.A. members will have to be registered by a member of the executive committee; this also applies to visitors from abroad. A large number of such colleagues are being invited, particularly those associated with the International Association of Small-Animal Specialists. Applications for accommodation at the Shaftesbury Hotel should be made through Thomas Cook & Son, Ltd., Berkeley Street, Piccadilly, London, W.1, stating whether the applicant is a member of the B.S.A.V.A. or not. Further details regarding the congress may be obtained from the Honorary Secretary, B.S.A.V.A., W. B. Singleton, Pentlands, Moulton Road, Kennett, Nr. Newmarket, Suffolk.

We hope to publish a detailed programme a little later on.

THE ASSOCIATION OF VETERINARY STUDENTS

The 1958 Conference of this Association will be held in Bristol from January 24th to 26th. It will be opened by Sir Philip Morris, vice-Chancellor of the University, and Professor C. W. Ottoway. A full programme includes lectures on "The Future of the Veterinary Profession," by Dr. E. L. Taylor and Mr. J. B. White; two lectures on reproduction respectively by Mr. D. R. Melrose and Mr. J. P. Frappell; visits to the National Stud, Dartington Hall, the Severn Wildfowl Trust at Slimbridge, and the A.R.C. research station at Long Ashton.

There will also be a number of sporting fixtures and social events, with the Association's annual general meeting on the final day.

THE UNIVERSITY OF LONDON

Special University Lectures in Veterinary Science

A course of two lectures on "Problems Associated with Large-animal Surgery," by Professor J. G. Wright, Dean of the Faculty of Veterinary Science and Professor of Veterinary Surgery in the University of Liverpool, will be given at the Royal Veterinary College at 4 p.m. on February 21st and 28th. The titles of the lectures will be "Equine Anaesthesia" and "Bovine Dystocia." At the first lecture the chair will be taken by Dr. K. G. Lloyd-Williams, Dean of the Royal Free Hospital School of Medicine and Dean of the Faculty of Medicine in the University of London.

The lectures are addressed to students of the University and to others interested in the subject; admission is free, without ticket.

UNIVERSITY NEWS

Bristol

A dissertation submitted by Mr. P. M. Biggs, Lecturer in Veterinary Clinical Pathology, has been approved for the degree of Doctor of Philosophy. The thesis was entitled "Lymphoid tissue in the endocrine glands of the domestic chicken: its significance in health and disease."

Liverpool

Degree of B.V.Sc. Third Examination

PART I. PHARMACOLOGY. JANUARY, 1958.

Bird, Christine M.; Butterfield, W. E.; Hamilton, J. G.; and Nyavor, A.

A NEW PROPHYLACTIC TRYPANOCIDE

Details of a new drug for the control of trypanosomiasis having just been made available to the agricultural and other press, our readers may be interested in the following note, for which we are indebted to Mr. W. M. Brownlie.

A new prophylactic drug for the control of trypanosomiasis in cattle has just been introduced by Boots Pure Drug Co. Ltd. The drug, 2 amino-7-(2 amino-6-methyl-4 pyrimidylamino)-9-*p*-aminophenylphenanthridine 10:1′-dimethobromide,* was known during the period of field trial in Africa as R.D.2801. It was discovered at Nottingham while following up work on Ethidium, the curative trypanocide developed in the same laboratory, which has proved valuable in the treatment of infection with *T. congolense* and *T. vivax*.

Extensive field trials in Africa have shown that a single dose of the new drug may give protection in the field for as long as 6 months.

* Prothidium.

R.C.V.S. OBITUARY

We record with regret the deaths of the following members of the profession:—

GARDEN, George, 189, Station Road, Wylde Green, Sutton Coldfield, Warwicks. Graduated May 28th, 1900, at the Royal (Dick) Veterinary College, Edinburgh. Died December 20th, 1957.

GLOVER, Richard Clarke, V.D., c/o Glynn, Mills & Co., Kirkland House, Whitehall, London, S.W.1, Major late R.A.V.C., Major Rangoon Light Horse (A.F.I.). Graduated May 7th, 1904, at the Royal Veterinary College, London. Died December 8th, 1957.

HAMILTON, Alexander Penn, 21, Halbeath Road, Dunfermline. Graduated December 14th, 1926, at the Royal (Dick) Veterinary College, Edinburgh. Died January 8th, 1958, aged 53 years.

LEYLAND, A. Harold, Aspinall Street, Prescot, Lancs. (Captain late R.A.V.C. (T.F.)). Graduated Edinburgh, December 23rd, 1905. Died January 11th, 1958, aged 78 years. The funeral took place at Prescot on January 14th.

PEACH, Charles John, Dove House, Mayfield, Ashbourne, Derby, Captain late R.A.V.C. Graduated January 26th, 1918, at the Royal Veterinary College, London. Died November 4th, 1957.

PERSONAL

Birth

LEWIS.—On January 3rd, 1958, at University College Hospital, London, to Sheila, wife of Derek Lewis, M.R.C.V.S., Rochester, a son, Mark Quentin, brother for Wendy and Jayne.

A DISTINGUISHED VISITOR

A distinguished guest at the R.C.V.S. Council meeting held on January 10th was Dr. F. W. Schofield, formerly professor and Head of the Department of Pathology of Ontario Veterinary College. In welcoming him the President said he was undoubtedly known not only by his great reputation in the other hemisphere, but by his many and varied contributions to veterinary science. He was known to many members of the profession because of the extreme and very kind hospitality he had dispensed to members from Britain who had visited Canada over many years. His recent tour to Europe had included countries beyond the Iron Curtain and he had many contacts throughout the world.

Dr. Schofield, in reply, expressed his thanks for being invited to see Council in session. On his return home, he would report the kindness which had been extended to him. He complimented the Council on appointing his good friend Mr. George Gould to the honourable position of President. The Canadian College had been founded by a graduate from Edinburgh, who was followed by an Englishman, another Scot, and now a Welshman. The Canadians had, therefore, tried to be loyal to all the components of the United Kingdom.

THE REGISTER OF VETERINARY SURGEONS

The names of the under-mentioned members have been removed, at their own request, from the Register of Veterinary Surgeons as from January 14th, 1958: BALLEK, Jan Charles (Commonwealth List), 148, Mount Street, Coogee, Sydney, N.S.W., Australia; CORDY, Charles H., c/o Dr. Kidd, 367, Commercial Road, Maritzburg, Natal, South Africa; FORREST, James, St. Helens, Melrose, Roxburghshire.

COMING EVENTS

January

22nd (Wed.). Winter Meeting of the North of Scotland Division in the Northern Hotel, Aberdeen, 2.30 p.m.

23rd (Thurs.). Council Meeting of the Society of Practising Veterinary Surgeons at 7, Mansfield Street, London, W.1, 5 p.m.

24th (Fri.). Annual General Meeting of the Mid-west Division, Berkeley Café, Bristol, 2.15 p.m.

25th (Sat.). Meeting of the B.S.A.A., Southern Area, at the Royal Hotel, Winchester, 7.30 p.m. (dinner). 8.30 p.m. meeting.

29th (Wed.). Meeting of the B.S.A.A. Midland Region at the Radbrook Hall Hotel, Radbrook Road, Shrewsbury, 2.30 p.m.

Ordinary General Meeting of the Southern Counties Veterinary Society at the Red Lion Hotel, Salisbury, 7 p.m.

31st (Fri.). Annual General Meeting of the Yorkshire Veterinary Society in the Hotel Metropole, Leeds, 1, 2.30 p.m.

February

5th (Wed.). General Meeting of the Midland Counties Veterinary Association at the Birmingham Medical Institute, 36, Harborne Road, Birmingham, 15, 2.45 p.m.

Meeting of the Lancashire Veterinary Association in the University Veterinary Hospital, Liverpool, 2.30 p.m.

6th (Thurs.). General Meeting of the Central Veterinary Society at the Royal Veterinary College, Camden Town, N.W.1, 6 p.m.

7th (Fri.). Annual Ball of the Royal (Dick) School of Veterinary Studies in the Assembly Rooms, George Street, Edinburgh, 9 p.m.

Annual Ball of the Glasgow University Veterinary Medical Association in the Rhul, Sauchiehall Street, Glasgow, 8 p.m.

14th (Fri.). General Meeting of the Society for the Study of Animal Breeding at the B.V.A., 7, Mansfield Street, Portland Place, London, W.1, 11 a.m.

Joint Meeting of the Society of Practising Veterinary Surgeons and the Shropshire Veterinary Club at the Radbrook Hall Hotel, Shrewsbury, 7.30 p.m.

General Meeting of the Society of Practising Veterinary Surgeons in the Radbrook Hall Hotel, Shrewsbury, 8 p.m.

20th (Thurs.). Ordinary Meeting of the Ayrshire Veterinary Association in the Ailsa Lounge, Ayr Station Hotel, 2.30 p.m.

B.V.A. COUNCIL AND COMMITTEE MEETINGS

Wednesday, January 22nd, 1958, at No. 7, Mansfield Street, W.1.

10.00 a.m. Veterinary State Medicine Committee.
11.30 a.m. Small-Animals Committee.
2.00 p.m. Farm Livestock Committee.

Thursday, January 23rd, 1958, at No. 7, Mansfield Street, W.1.

10.00 a.m. Parliamentary and Public Relations Committee.

11.30 a.m. Home Appointments Committee.
12.30 p.m. Finance Sub-committee.
2.15 p.m. General Purposes and Finance Committee.

Friday, January 24th, 1958, at the Connaught Rooms, W.C.2.

10.30 a.m. Council Meeting.

FOOT-AND-MOUTH DISEASE

The areas described in the schedules below are declared to be Infected Areas for the purpose of preventing the spread of foot-and-mouth disease:—

So much of the City and County Borough of Salford as lies to the north of the railway running from Astley *via* Patricroft, Eccles and Cross Lane to Manchester (Victoria), excluding the said railway.

The County Borough of Bolton.

IN THE COUNTY OF LANCASTER

The Boroughs of Eccles, Farnworth, Leigh, Prestwich, Radcliffe and Swinton and Pendlebury.

In the Petty Sessional Division of Bolton: The parishes of Little Lever, Kearsley, Little Hulton, Horwich, Blackrod and Westhoughton.

In the Petty Sessional Division of Bury: The parish of Whitefield.

In the Petty Sessional Division of Leigh: The parishes of Atherton, Tyldesley and Golborne.

In the Petty Sessional Division of Warrington: The parishes of Croft, Rixton-with-Glazebrook and Woolston.

In the Petty Sessional Division of Manchester: The parishes of Worsley, Irlam, Flixton, Urmston and Davyhulme.

In the Petty Sessional Division of Wigan: The parishes of Haigh, Aspull and Hindley.

IN THE COUNTY OF CHESTER

In the Petty Sessional Division of Altrincham: The parishes of Warburton, Partington and Carrington.

In the Petty Sessional Division of Chester Castle: The parishes of Lower Kinnerton, Dodleston, Marlston cum Lache, Claverton, Eccleston, Eaton, Huntingdon, Saighton, Pulford and Poulton.

In the Petty Sessional Division of Broxton: The parishes of Buerton, Churton Heath, Lea Newbold, Golborne David, Handley, Aldford, Edgerley, Churton by Aldford, Churton by Farndon, Farndon, Kings Marsh, Coddington, Aldersey, Barton, Clutton, Carden, Stretton, Crewe, Caldecott, Grafton, Church Shocklach, Horton, Chorlton, Shocklach Oviatt, Cuddington, Threapwood, Newton by Malpas and Oldcastle.

IN THE COUNTY OF DENBIGH

The Borough of Wrexham.
The Petty Sessional Divisions of Bromfield and Ruabon.

IN THE COUNTY OF FLINT

The Petty Sessional Division of Hope.
In the Petty Sessional Division of Maelor: The parishes of Worthenbury, Bangor, Overton, Penley, Halghton and Willington.

IN THE COUNTY OF NORFOLK

In the Petty Sessional Division of North Erpingham: The parishes of Antingham, Trunch, Mundesley and Suffield.

In the Petty Sessional Division of South Erpingham: The parishes of Wickmere, Itteringham, Erpingham, Alby with Thwaite, Colby, Oulton, Blickling, Ingworth, Cawston, Aylsham, Tuttington, Marsham, Brampton, Skeyton, Swanton Abbot, Hevingham, Buxton with Lammas, Scottow, Stratton Strawless, Coltishall and Belaugh.

In the Petty Sessional Division of Tunstead and Happing: The parishes of Felmingham, Knapton, Paston, Swafield, North Walsham, Bacton, Witton, Honing, Worstead, Happisburgh, East Ruston, Dilham, Brumstead, Lessingham, Smallburgh, Stalham, Ingham, Ashmanhaugh, Barton Turf, Neatishead, Hoveton, Tunstead, Sloley and Westwick.

In the Petty Sessional Division of Eynsford: The parishes of Sall, Reepham, Sparham, Booton, Little Witchingham, Brandiston, Haveringland, Lyng, Alderford, Great Witchingham, Swannington, Weston Longville, Morton on the Hill and Ringland.

In the Petty Sessional Division of Forehoe: So much of the parishes of Easton and Honingham as lies to the north

of the main road running from Norwich to Hockering, excluding the said road.

In the Petty Sessional Division of Taverham: The parishes of Attlebridge, Felthorpe, Taverham, Drayton, Horsford, Hainford, Frettenham, Horstead with Stanninghall, Hellesdon, Horsham St. Faith and Newton St. Faith, Catton, Spixworth, Crostick, Wroxham, Sprowston, Beeston St. Andrew, Salhouse, Rackheath and so much of the parish of Costessey as lies to the north of the main road running from Norwich to Easton, excluding the said road.

In the Petty Sessional Division of Mitford and Launditch: So much of the parishes of East Tuddenham and Hockering as lies to the north of the main road running from Norwich to North Tuddenham, excluding the said road.

IN THE COUNTY OF DORSET

In the Petty Sessional Division of Dorchester: The parishes of Minterne Magna and Buckland Newton.

In the Petty Sessional Division of Sherborne: The parishes of Hilfield, Hermitage and Glanvilles Wootton.

CORRESPONDENCE

The views expressed in letters addressed to the Editor represent the personal opinions of the writer only and their publication does not imply endorsement by the B.V.A.

Nematodirus battus in Cattle

Sir,—In their recently published list* of the gastro-intestinal nematodes of British cattle, Morgan and Soulsby recorded 2 species of Nematodirus, namely *N. filicollis* and *N. helvetianus*. Subsequently T. E. Gibson pointed out that *N. spathiger* should have been added.

It now appears that *N. battus* should also be listed, recent observations having shown that this species, though so far only recognised as a parasite of sheep, can, in fact, parasitise cattle and that it does so in Britain.

The distinctive eggs were encountered in the faeces of several calves grazing an experimental paddock at various times, and when one of these calves was slaughtered the worms recovered from its small intestine were examined and both male and female specimens of *N. battus* identified.

The calf from which these worms were recovered had been reared under conditions calculated to prevent accidental infection with worms. It was put out on the paddock on October 15th, 1957. Since the paddock had been grazed by calves only and no sheep had had access to it since March, 1956, it would seem probable that the infection can be maintained by cattle alone.

The eggs of *N. battus* have also been recognised in the faeces of several calves grazing on other experimental paddocks, and more recently they have been seen in faeces samples taken for other purposes from cattle on commercial farms.

Yours faithfully,
J. W. PARFITT,
J. F. MICHEL.

Ministry of Agriculture Veterinary Laboratory,
Weybridge.

January 10th, 1958.

* MORGAN, D. O., & SOULSBY, E. J. L. (1956). *Vet. Rec.* **68**. 1,029.

The Use of Chlorpromazine Hydrochloride in Oesophageal Obstruction

Sir,—Under the sub-heading Choke in Cattle, in their paper "Some Observations on the Use of Chlorpromazine Hydrochloride in Ruminants," Martin, Simpson, and Reid wrote: "A distinct impression of oesophageal relaxation was gained"—*i.e.* after the injection of Largactil.

I believe that an intravenous injection of 25 mg. Largactil made it possible, by such relaxing action, for an Alsatian dog to pass an obstructing bone from the thoracic oesophagus, into the stomach.

The owner had reported, 2 hours before my examination, that she believed the dog had just swallowed something and was trying to vomit. From her description of the symptoms, and my examination, it appeared to be a typical case of thoracic oesophageal obstruction.

To facilitate transporting the dog to the surgery, Largactil was given intravenously.

Within a few minutes the Alsatian became extremely restive and began tearing frantically at a settee with its front claws. This continued for about three minutes, and then the dog lay down, rather exhausted, presumably under the sedative action of the drug.

After this episode I decided to leave the dog at its own home, and make tentative enquiries regarding the possibility of it being operated on at Liverpool University Veterinary Hospital, the following day.

However, when I telephoned the owner that evening, she said that the Alsatian had drunk some water without regurgitation, and appeared much more normal. By the time of my visit the next day, the dog had taken soft food and retained it. Without further treatment, it continued in normal health.

I am convinced that in this, an early case of oesophageal obstruction, the Largactil caused a sufficient relaxation of oesophageal muscle to allow the bone to pass into the stomach, though not without causing a considerable degree of pain to the dog.

Yours faithfully,
C. STEELE.

65, Seaview Road,
Wallasey,
Cheshire.

January 9th, 1958.

Muscle Relaxants

Sir,—I am delighted to learn from Dr. Montgomerie's letter that an organisation of the high repute of the Wellcome Research Laboratories is to put on the market a drug which will avoid much of the physical risk and mental torture to the veterinary surgeon, associated with the accepted methods of casting the horse.

I have diligently read all your correspondence on the rights of animals. By and large my reaction to those letters which appear to make a fetish of such rights have been somewhat cynical. While I am prepared to concede to animals the right to humane

treatment at all times, I am even more ready to concede to man the right to protection from physical risk and mental anguish.

Perhaps only those of us who are gifted by nature with a strong sense of physical and mental fear derived from a too-vivid imagination, can grasp the poignancy of Dr. Montgomerie's expression. On the other hand, people so constituted will be the first to do all that should be done to avoid unnecessary pain to the patient.

Yours faithfully,
J. P. PICKERING.

Orchard House,
Priestpopple,
Hexham,
Northumberland.

January 11th, 1958.

The Treatment of Bovine Ketosis

Sir,—I read with great interest Mr. Paterson's article on prednisolone in the treatment of bovine ketosis. During last summer I was fortunate enough to have seen practice with Dr. J. L. McAuliff of New York State, who had much confidence in the efficacy of prednisone in the treatment of this condition. However, it appeared to me that he only used this drug where the ketosis was severe. In other cases conventional treatment was used.

In one cow which showed ketosis following a retained placenta he gave 100 mg. of prednisone intravenously and 200 mg. intramuscularly. In another case where the ketosis was primary he administered 300 mg. prednisone intramuscularly. Both cows recovered completely.

Dr. McAuliff sometimes used prednisone (100 mg. intravenously) together with calcium borogluconate in the treatment of milk fever, though again it appeared to me that such treatment was used only in severely "shocked" animals.

Prednisone and also prednisolone acetate were used by Dr. John Steele in the treatment of lameness in Standard-bred horses at Vernon Downs race-track. The doses used in these cases were in the order of 200 mg. of prednisone intramuscularly.

Cortisone and cortisone-like compounds are very much in vogue in the United States at the present time. Many firms manufacturing antibiotics include hydrocortisone in their preparations. The main drawback seems to be the high cost.

Yours faithfully,
R. B. BLATCHER.

School of Veterinary Medicine,
Madingley Road,
Cambridge.

January 11th, 1958.

Box Numbers

Sir,—As a recent graduate may I presume to join with Mr. Crosfield in deprecating this recent increase in the use of box numbers in the appointments vacant columns?

I, together with, I imagine, the majority of final year students and new graduates, have recently taken more than a passing interest in these columns and have found that a normally anxious time has been made even more frustrating due to so many advertisers resorting to this cloak of secrecy. In the issue of January 4th, out of 50 insertions under the appointments vacant heading, 32 appeared under box numbers, 7 of which achieved the ultimate in incognisance by not even mentioning the county of origin!

This, I am sure, can only lead to delay and frustration, not only for those on the labour market but for the advertisers themselves. May I, therefore, appeal to future advertisers who feel the need of using a box number at least to include the county in their advertisement?

Yours faithfully,
TREVOR TURNER.

15, Mandeville Road,
Northolt,
Greenford,
Middlesex.

January 9th, 1958.

DISEASES OF ANIMALS ACT, 1950—GREAT BRITAIN

Summary of Returns of Confirmed Outbreaks of Scheduled (Notifiable) Diseases

Period		Anthrax	Atrophic Rhinitis	Foot-and-Mouth	Fowl Pest	Sheep Scab	Swine Fever
16th to 30th November, 1957		9	—	10	81	—	33
Corresponding period in	1956	21	—	11	98	—	33
	1955	34	—	1	110	—	57
	1954	23	—	—	58	—	42
1st January to 30th November, 1957		299	8	135	897	—	885
Corresponding period in	1956	1,218	11	146	771	—	700
	1955	721	6	7	624	—	1,331
	1954	303	4	12	717	—	1,336